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DETERMINISTIC AND STOCHASTIC SIR MODEL OF HIV IN GHANA

A Thesis

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by

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ABSTRACT

In this thesis, deterministic and stochastic differential equation (SIR) models for HIV propagation are formulated using Ghana data. The stability of the disease free and endemic equilibrium points of the models are investigated as well as an implementation of numerical simulation of the models to observe the effect of a decrease in the infection rate. It was found that for both the deterministic and the stochastic models, an infection rate of $\beta = 0.2$ or less would cause the number of infectives to be permanently less than the number of susceptibles.

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DEDICATION

To my lovely mother, Madam Grace Mamiley and Father, Mr. Sammy Amponsah Sacrifice

DECLARATION

I hereby declare that this submission is my own work towards the MSc. And that, to the best of my knowledge, it contains no material previously published by another person nor materials which has been accepted for the award of any other degree of the university, except where due acknowledgement has been made in the text.

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CHAPTER 1

INTRODUCTION

1.1 INTRODUCTION

In this chapter, we will discuss the background of HIV and state the problem statement. We will also discuss the mathematical methods that would be employed in our study.

1.2 BACKGROUND

HIV (human immunodeficiency virus) is the virus that causes AIDS. This virus can be passed from one person to another when infected blood, semen, or vaginal secretions come in contact with an unlimited person's broken skin. Also, infected pregnant women can pass HIV to their baby during pregnancy or delivery, as well as through breast-feeding (www.wikipedia.org).

People with HIV have what is called HIV infection and may develop AIDS as a result of their infection. The earliest known case of HIV-1 in a human was found in a blood sample collected in 1959, from a man in Kinshasa, Democratic Republic of Congo (www.cdc.gov).

Genetic analysis of this blood sample suggested that HIV-1 may be stemmed from a single virus in the late 1940s.

In somewhere the mid-1970s, United States discovered the virus. Doctors in Los Angeles and New York had cases of pneumonia, cancer, and other illness in a number of male patients who have had sex with other men. These conditions were not usual in people with healthy immune systems.

In 1982, public health officials began to use the term 'acquired immunodeficiency syndrome' or AIDS, to describe the occurrences of opportunistic infections (a kind of cancer).

HIV is a retrovirus and like most of the viruses in this family of viruses, the retroviridae, only replicate in dividing cells. Infection by the virus HIV-1, the most common variety, has many highly complex characteristic, most of which are still not understood. One such complexity is that the disease progression can last more than 10 years from the first day of infection. Another is that whilst most viral infections can be eliminated by an immune response, HIV is only briefly controlled by it (www.who.org).

The introduction of powerful anti-retroviral therapies has dramatically changed the progression time between HIV infection and the development of AIDS. Also other treatments can prevent or cure some of the illnesses associated with AIDS, but do not cure the AIDS itself.

People with HIV may experience these symptoms

- rapid weight loss
- recurring fever or profuse night sweats
- profound and unexplained fatigue
- swollen lymph glands in the armpits, or neck
- diarrhea that lasts for more than a week
- pneumonia
- memory loss, depression, and other neurological disorders

However, these signs alone are not sufficient for one to think that he has the disease, but then, the only way to know your HIV status is to be tested for HIV infection.

HIV testing and counseling provides an opportunity for infected individual to know their HIV status, and if infected, to access medical treatments that may help delay disease progression.

The only surest way of protecting oneself from contracting HIV is to abstain from sexual intercourse or to be in long-term mutually monogamous relationship with a partner who has been tested and known to be uninfected. Also consistent and effective use of condoms provides a high degree of protection against transmission of HIV. However, the use of condoms cannot provide absolute protection against HIV (www.medicineNet.com).

1.3 STATEMENT OF THE PROBLEM

HIV-1, the most common variety, has many highly complex characteristics, most of which are still not understood by researchers, and has therefore become a major public health problem worldwide. The fact that the disease progression can last more than 10 years from the first day of infection, and also like most viral infection which are eliminated by an immune response, HIV is briefly controlled by it. Africa is the most affected continent in the world in terms of HIV infection, yet not much has been done in terms of using mathematical modeling as a tool in finding solutions to the disease, especially in sub-Sahara Africa where the situation is escalating. It is against this background that we formulate a deterministic and stochastic differential equation model, with some parameter values from Ghana that helps us to understand the HIV propagation in Ghana.

1.4 OBJECTIVES OF THE STUDY

The objectives for this thesis are:

- To formulate a deterministic and stochastic differential equation models for HIV propagation.
- To investigate the stability of the equilibrium points of the models.
- To implement numerical simulation of the models.
- To determine the implications of these models in relation to the intervention in controlling the disease.

1.5 METHODOLOGY

1.5.1 Mathematical Methods

In this work, a deterministic SIR epidemic model will be formulated and use to determine the equilibrium points and the stability of these equilibrium points. A stochastic version of the deterministic SIR model would be considered, and its local stability and phase portrait implemented. In order to get realistic results, parameters for the model such as Death rate, rate of infection and Removal rate were obtained from the Ghana Health Service and CIA World Factbook (demorgraphic statistics) and were fitted into the model to find the equilibrium points. The stability of these points were then determined.

1.5.2 Computer Methods

Matlab software will be used to for the following computations;

- For finding the eigenvalues of the linearized system and their system.
- To identify the stability type using the eigenvalues.
- For plotting the Phase portraits and the trajectories of the equilibrium points
- For the numerical simulations of the deterministic and the stochastic version of the SIR epidemic model

1.6 JUSTIFICATION OF THE STUDY

Mathematical model has serve as an aid to understanding the dynamics of infectious diseases and how to control them. Therefore, in order to control the HIV/AIDS disease, one needs to understand the dynamics of the disease, and this can be done by matter of mathematical model.

1.7 ORGANISATION OF THESIS

This thesis begins with Chapter 1 in which the background of HIV is given. Chapter 2 is a review of a research work pertaining to HIV models that has been done. In Chapter 3 a Deterministic and Stochastic model of HIV is presented which explains the transmission dynamics of HIV. In chapter 4, the numerical simulation results of the models are presented. Finally in Chapter 5 we conclude the thesis with conclusion and recommendation.

CHAPTER 2

LITERATURE REVIEW

2.1 INTRODUCTION

In this chapter, we will discuss the biology and ecology of the HIV virus, as well as its life cycle in the cell of human. We will also discuss the social and the economic impart of HIV on the society. Finally, we will discuss the history of mathematical models, and the variant models of infectious diseases that have been proposed. We will also discuss the contribution of these models in regards to controlling infectious diseases and HIV specifically.

2.2 BIOLOGY AND ECOLOGY OF HIV VIRUS

HIV (human immunodeficiency virus) is the virus that causes AIDS. This virus can be passed from one person to another when infected blood, semen, or vaginal secretions come into contact with an uninfected person's broken skin. Through breast-feeding, the virus can also be passed on from mother to child.

HIV, like all viruses, is composed of a core and a protein coat. Its genetic material is stored in its core. The genetic material of all animals (humans and bacteria), is coded in the nucleus of the cell. The chemical in the nucleus that maintains this genetic code is called nucleic acid. Humans, plants and other microorganisms have two types of nucleic acids: ribonucleic acid(RNA) and deoxyribonucleic acid(DNA).Viruses, on the other hand, have either DNA or RNA(Consuelo and Caridad, 2004).

HIV's nucleic acid is RNA; Hence HIV is called an RNA virus. The protein coat of HIV carries the chemicals that enable HIV to enter cells. Once it enters the cell, HIV uses the cell's machinery to produce energy and reproduce itself.HIV uses an enzyme called reverse transcriptase, to make a DNA copy of its RNA and inserts it into the host cell's DNA.Viruses that can make a DNA copy from RNA are called retroviruses, because they reverse the usual process.HIV is a retrovirus and like most of the viruses in this family of viruses, the retroviridae, only replicates in dividing cells (www.cdc.gov).

HIV's DNA carries codes for nine genes, which are sections of nucleic acids that determine a trait or characteristics of a living being. Three of these genes, gag, pol, and env contain information needed to make structural protein for new virus particles. Also the genes, tat, rev and nef are regulatory genes, and the other three genes vif, vpr and vpu are auxiliary (helper) genes.

The auxiliary genes contain needed information of protein that HIV uses to infect a cell and make new copies of it. Retroviral infections do not kill the cells that they infect, but then, many of these viruses cause cancer to the cells that they infect. The family of retroviruses to which HIV belongs does not cause cancers directly (Pratt, 2003).

HIV infects vital white blood cells in the human immune system such as lymphocytes or CD4 T-cells, dentritic cells and macrophages.HIV infection leads to low level of CD4 T-cells. These happen as a result of the increased rates of apoptosis in infected cells, and viral killing of infected cells as well as killing of CD4 T-cell (Murray, 2002).

HIV infections are of two types, HIV-1 and HIV-2.HIV-1, the most common cause of the majority of HIV infections, has many complex characteristics, most of which are still not understood by researchers. One of such characteristics is that the disease progression can last

more than 10 years. Another is that whilst most of viral infections can be eliminated by an immune response, HIV is briefly controlled by it. The depletion of CD4 T-cells in the immune system leads to AIDS (http://www.who.org).

2.3 THE HIV LIFE CYCLE

HIV passes through several stages in order to infect a person. These stages include binding to the cell, fusing with the cell membrane, replicating itself with reverse transcription, and releasing new viruses from the cell. HIV infects a person by first attaching its virus to a cell at a specific binding site. Thus, HIV can only attach to cells with the appropriate type of binding site. The CD4 surface molecules of the helper Tcells are the main binding sites for HIV (Pratt, 2003).

All primate lentiviruses use CD4 as a binding site to bind to the T cells or macrophages.HIV and lentiviruses attach mostly to T lymphocytes, and are therefore called T lymphotropic.Another receptor of HIV virus is Chemokine co-receptors (CCRs).CCRs assist T cells, providing a place for Cytokines and other chemicals to attach. These chemicals are directed to Microorganisms to which they bind.HIV membrane gp120 binds first to CD4, and then to CCR-5 or another CCR.HIV also uses the CCRs cells in the cervix and the large intestine as binding sites(Consuelo and Caridad,2004).

Fusion takes place after the binding process. The membrane of the HIV and the cell combine. The HIV virus then makes copies of itself. During reverse transcription, the enzymes called reverse transcriptase makes a DNA copy of HIV's RNA; this DNA is inserted into the person cell as a provirus, which remains inactive in the cell's genetic material until the cell is activated(Murray,2002).

The HIV proteins are broken down into active proteins by enzymes called proteases and are organized into incomplete virus particle. The virions bud from the cell then combines with tiny pieces of the cell membrane to form a mature virus particle which can infect. If the cell is not activated and does not divide itself, no virions are made. This state of remaining dormant in the cell DNA is called the latent (inactive) period of the disease. This can take about 5 to 10 years about which the patient shows no symptoms of the disease, but can infect others (http://www.findarticle.com).

2.4 EPIDEMIOLOGY OF HIV

Epidemiology may be defined as the study of the transmission dynamics of infectious diseases with the objective of tracing factors that contribute to the dynamics and stability of the disease under consideration (www.wikipedia.org).

Mathematical models have been used in the study of epidemiology, and these models have served as an aid to understanding the transmission dynamics of infectious diseases.

HIV has gone to the fore-front of epidemiological research ever since its discovery. Its transmission dynamics, and how to control it, has been of great concern to public health globally. Many consider HIV to be the most serious world epidemics of this century. Though many works have been done in the field, yet much is still unknown about HIV.

2.5 HISTORY OF HIV

The first known case of HIV-1 in humans was found in a blood sample of a man in Kinshasa, Democratic Republic of Congo in the somewhere early1959.

It was believed that these viruses originated from Chimpanzees living in West Africa. It has been explained that these viruses were passed on to humans as a result of human activities such as hunting and eating of bush meat (www.medicinenet.com).

United States discovered the disease somewhere 1970s, with gay men who have had sex with other men. It was reported that these men have developed pneumonia, cancer, and other types of illnesses which were rare in people with healthy immune system (htt://www.cdc.gov).

In 1982, public health officials became concerned about the disease, and a formal surveillance of the disease began in the United States. The disease was then named 'acquired immunodeficiency syndrome', describing a condition in humans in which progressive failure of the immune system allows life-threating opportunistic infections and cancers to thrive (Consuelo and Caridad, 2004).

In 1983, the virus that causes AIDS was discovered, and was named HTLV-III/LAV (human T-cell lymphotropic virus-type III).The name was later changed to HIV (human immunodeficiency virus).

In 1985, the means to avoid becoming infected were known and a test for HIV infection was developed, allowing blood transfusions to be screened for the presence of HIV infection (Benenson, 1990).Then in 1987, the first truly effective drug that suppressed viral replication was developed and introduced into clinics, allowing infected people to get access. By the mid-

1990s, range of antiretroviral drugs attacking the virus at different stages of its replication cycle became available to treat HIV disease (http://www.sceinceaid.co.uk).

2.6 GLOBAL AND GEOGRAPHIC DISTRIBUTION OF HIV

HIV/AIDS, since its discovery in the year 1980s, has affected most parts of the world. The pandemic is seen as one of the world's most dangerous epidemic of all time. The statistics about the global distribution of HIV/AIDS world-wide are overwhelming.

The World Health Organization(WHO,2006), estimates that about 40 million people of the world's population are living with HIV/AIDS, and that nearly 25 million people have died of AIDS since the disease was first discovered.

The report indicates that 50% of all new HIV infections and 30 percent of the 40 million people are youth. While every nation has in some way been affected by this pandemic, it is Africa that the grip of HIV and AIDS has been, by far, the deadliest.

(World Bank, 2002), indicates that over two thirds of HIV/AIDS related deaths are from Africa. African countries like South Africa, Botswana, Malawi and Swaziland have much higher rates of HIV infection.

(UNESCO, 2002), report shows that almost one in every ten adults in sub-Saharan Africa are HIV positive.

Russia saw more new infections in 2000 than in all the previous years of the epidemic combined. The number of cases in Eastern Europe and Asia has risen by more than two thirds in the last year. The situation is alarming in the United States, with increase number of gay men and gay marriages, HIV infection is doubtlessly on the increase in the United States.

In the English-speaking Caribbean, it is the leading cause of death among 15-44 years old.

2.7 TRANSMISSION HYPOTHESIS OF HIV

HIV is primarily transmitted through shared bodily fluid such as blood, semen, or vaginal secretions, pre-ejaculatory fluid and saliva. Most people in the world have been infected with HIV as a result of being sexually exposed to the virus. This is due to the fact that HIV is present in seminal, pre-ejaculatory, vaginal and cervical secretions, and in saliva of infected individual. Variety of sexual behaviors like homosexual and heterosexual facilitate this viral transmission,

Also, infected pregnant woman can pass HIV to their baby during pregnancy or delivery, as well as through breast-feeding (http://www.sceinceaid.co.uk)

2.8 BURDEN OF HIV

HIV/AIDS has a whole lot of negative impact on the individual and the society in a number of ways.

First increased morbidity and mortality are likely to have significant impacts on national economies.HIV infection can lead to reduction in Gross domestic product of a nation. (Action Aid,2003),indicates that skilled workers who get themselves infected with HIV,are more likely to be fired by their employers or leave the job as a result of the stigma. The potential for labor substitution crucially affects the degree to which any loss of time is translated into a loss of output. Similarly in the industrial and service sectors, other members of the workforce may cover to some extent for sick colleagues. Even if market output is maintained, there may be costs associated with labor substitution, depending on the value of the activities from which the substituting labor is withdrawn (UNAIDS/WHO, 2004).

Unemployment and underemployment are common features of sub-Saharan economies, and farming is often undertaken communally, in households or extended families. In the event of temporary disability of a household member, the family workforce may provide a cushion for the period of absence of the disabled member, limiting the consequent loss of output. During some seasons, agricultural underemployment may be so prevalent that the time lost by sick individuals can be fully compensated for.

The simple presence of HIV/AIDS in a community or country also hampers individual and national prosperity due to its influence on social and economic decisions (htt//:www.cdc). The risk of contracting HIV/AIDS in endemic areas can deter investment, both internal and external. It affects individual and household decision making in many ways that have a negative impact on economic productivity and growth. Some of the impacts are undeveloped tourist industry due to reluctance of travelers to visit HIV/AIDS-endemic areas.

HIV infection also has a negative effect on the standard of Education on a nation. Teachers and pupils who get infected with HIV eventually lose focus with regards to their responsibility as teachers or students. These attitudes have effects on the educational objectives in general. UNECA (2000) presents reports from Kenya (teacher deaths rising from 450 in 1995 to 1,500 in 1999), Congo (schools closing due to death of teachers from AIDS).

2.8.1 Economic and Social implication of HIV

According to Pratt (2003), "The burden of HIV/AIDS is enormous, on global scales, HIV/AIDS disease is among the leading causes of preventable ill-health and death in people in developing countries, causing approximately 11million illness and more than 5 million deaths each year. In Every day more than 2000 lives are lost worldwide due to HIV. These estimates render HIV the

pre-eminent world viral disease and one of the top three killers among Communicable diseases." Beyond mortality, HIV causes morbidity through weakness, malnutrition, anemia, unexplained prolonged fever, chronic diarrhea, spleen diseases and vulnerability to other diseases. The health consequences of HIV vary in terms of severity, but the global impact of HIV on human health, productivity, and general well-being is profound (http://www.hab.hrsa.gov).

HIV imposes substantive social and economic costs. It impedes economic development through several channels, including but certainly not limited to, quality of life, fertility, population growth, saving and investment, worker productivity, premature mortality and medical costs (http://www.BNF.org).

The various effects of HIV are outlined below:

2.8.2 Mortality

Estimating the number of deaths due to HIV/AIDS is problematic (UNAIDS/WHO, 2003). It is perhaps not surprising that most studies do not attempt to capture any of the economic effects of death, focusing on the implications of morbidity alone. However, a wide range of immediate and long-term effects are thus excluded, ranging from funeral costs, to lost output of the deceased, subsequent changes in the organization of activities, and potentially the dissolution of the household or knock-on effects on the health of other household members (Falola and Heaton,2007).

2.8.3 Malnutrition

Malnutrition is a common features of human immunodeficiency virus (HIV) disease and further compounds patient problems and immune system incompetence. Weight loss and thinness are common in all stages of HIV disease in Africa and the Western world. Infection by HIV produces a progressive, involuntary weight loss in the early stages of the HIV disease and

increases in severity as the disease progresses (Pratt, 2003).HIV disease also causes metabolic changes and deficiencies of some nutrients, vitamins and minerals which cause illnesses in infected individual (Taylor,1994).

HIV disease has a significant impact on nutritional status of the individual resulting in malnutrition. Malnutrition in turn causes decreased immune function, increased morbidity and mortality and finally decreased the quality of life in the individual with HIV (www.cdc.gov).

Malnutrition also decreases the ability to withstand opportunistic events and prolongs periods of hospitalization (Gorbach, 1999).People with malnutrition have decrease in self-care ability and therefore have to depend on other people like family members. The time lost by such people in taking care of these family members has impact on the family and the economy.

2.8.4 Interaction with other diseases

In addition to its direct role in morbidity and mortality, HIV/AIDS is also thought to have a significant indirect effect in conjunction with other common diseases such as tuberculosis, diarrheal disease and malnutrition, although the extent of the indirect impact is difficult to measure and not well understood(stillcutt,2004).

2.8.5 Intellectual Development

HIV encephalopathy: A clinical finding of disabling cognitive or motor dysfunction interferes with activities of daily living such as school absenteeism although the evidence is less. Variations in reasoning ability, cognitive skill, and years of schooling are considered to be important determinants of future variations in productivity and earnings of individuals (Knight and Sabot, 1990), so the economic impact is likely to be significant.

2.8.6 Economic Cost

Economists have attempted to put an economic value on the burden of HIV/AIDS by measuring the impacts on households and national economies (Boissier, Knight and Sabot, 1985).

2.8.7 Household

HIV imposes both direct and indirect costs at household level. Direct costs can be from a personal expenditure or a public expenditure. Personal expenditures include individual or family spending on doctors' fees, Anti-retroviral drugs, transport to health facilities, support for the patient and sometimes an accompanying family member during hospital stays. Public expenditures include spending by government on maintaining health facilities and health care infrastructure, education and research. In some countries with a heavy HIV burden, the disease may account for as much as 40% of public health expenditure, 30-50% of inpatient admissions, and up to 50% of outpatient visits (http://www.one.org/international).

The indirect costs of HIV include lost of productivity or income associated with illness or death. This might be expressed as the cost of lost workdays or absenteeism from formal employment and the value of unpaid work done in the home by both men and women. Indirect costs, which are typically harder to measure, include loss of work efficiency and time and work reallocation within the household. For children in particular, indirect costs also include nutritional deficiencies, cognitive and educational disabilities, and physical retardation. Pain and suffering are clearly substantial indirect costs but are perhaps most difficult to quantify and monetize. In general, long term effects such as child development and resistance are unknown (Hutubessy, Bendib and Evans, 2001). In the case of death, the indirect cost includes the discounted future lifetime earnings of those who die.

2.8.8 National Economies

HIV/AIDS is estimated to cause a decline in economic growth in the range of 0.25% to 1.3% of per capita Gross National Product (GNP) growth in tropical countries, even after accounting for initial endowments, overall life expectancy and geographic location. To the extent that slow economic growth limits funds for HIV/AIDS control, there is a vicious cycle of poverty and HIV diminishes economic opportunities for a large number of the world's inhabitants. HIV affects the health and wealth of nations and individuals alike. In Africa, HIV is a disease of poverty and a cause of poverty. For developing economies the gap in prosperity between countries with HIV and countries without HIV has become wider every single year. Annual economic growth in countries with high HIV transmission has historically been lower than in countries without HIV. Economists believe that HIV is responsible for a 'growth penalty' of up to 1.3% per year in some African countries. When compounded over the years, this penalty leads to substantial differences in GDP between countries with and without HIV and severely restrains the economic growth of the entire region.

2.9 HISTORY OF MATHEMATICAL MODELING OF INFECTIOUS DISEASES

The intuition that transmission of infectious diseases follows certain laws that can be modeled mathematically has existed long. In 1766, Daniel Bernoulli published an article where he mathematically analyzed the effects of smallpox variolation on life expectancy (Dietz and Heesterbeek, 2000).

Sir Ronald Ross, who received the Nobel Prize award for his contribution on elucidating the life cycle of the Malaria parasite, used mathematical modeling to investigate the effectiveness of various intervention strategies for Malaria (Ross, 1911).

Kermack and Meckendrick (Kermack and Mckendrick, 1991a, 1991b, 1991c), described the dynamics of disease transmission in terms of a system of differential equation, and opened up the concept of threshold quantities.However the nonlinear dynamics of infectious disease transmission came into the scene somewhere early twentieth century. Since then mathematical modeling has evolved as an interesting area in the field of applied mathematics, and has been of great help to public health in policy making.

The study of epidemics has come up with astonishing number of variety of models and explanations for the spread and cause of epidemic outbreak.In McNeil (McNeil, 1989), he explains the relation between disease and people. Another astonishing work in regards to epidemiological modeling is that of Oldstone (Oldstone, 1998).Oldstone described the various aspects of diseases from the triumphs of medicine to socioeconomic.

Modeling has been helpful in giving estimates for the level of vaccination for the control of transmitted infectious diseases.

(Anderson and May, 1982, 1985, 1991) discussed and estimated with the model the effects of different vaccination programmes.

2.9.1 COMPARTMENTAL MODELS IN EPIDEMIOLOGY

A compartmental model is one for which the individuals in a population are classified into compartments depending on the disease status with regard to the infection under study. Thus the individual may be classified as susceptible (S), infected (I), and removed (R) based on their status of the disease under consideration. For example, an SIR model describes a disease history of susceptible individual becoming infectious through interactions with an infected individual, and infectious individual moving into the removal class by either immunity or death. A

compartmental model for infection transmission with an *exposed* (or latent) compartment (explicitly containing those infected but not yet infectious) and lasting immunity would be called an *SEIR* model, and situations where susceptibility can return after infection (or after immunity) would be called an *SIS* (or an *SIRS*) model (Busenberg and Cooke,1993).

An example of an SEIR model is

$$\frac{ds}{dt} = \mu N - \beta C \frac{SI}{N} - \mu S$$

$$\frac{dE}{dt} = \beta C \frac{SI}{N} - (\gamma + \mu)E$$

$$\frac{dI}{dt} = \gamma E - (\rho + \mu)I$$

An equation for R in this model is not important since $N = S + E + I + R$ is constant. The model is an extension of the SIR model, not only because of the introduction of the exposed class, but also because of the host birth and deaths are included. Compartmental models have provided valuable insights into the epidemiology of many infectious diseases. Extensions to the models that have been presented here include an additional death rate due to the infection, re-entering the S after recovery or due to loss of immunity, a birth rate directly into the infective class and reduced fertility of infected individuals. Also, the ways in which births are modeled or transmission is described may influence the dynamic behavior of the model systems (Daley and Gani, 1999). The important assumption that can be made is homogenous mixing within compartments. If this does not apply heterogeneity must be an explicit feature of the model structure. The important quantity that must be determined is the basic reproduction number (R_0), as this provides the key to transmission dynamics, the ease by which major epidemics may be

prevented and prospects for the eradication of an infection. The concept of the critical community size may apply to the susceptible community in a population where the infection timescale is much faster than the demographic timescale. Here the infection (such as measles) may leave a small susceptible population following an epidemic, but births into the population increase the susceptible pool and effectively increase R_0 until another epidemic is triggered. In addition, temporal heterogeneity may manifest as seasonal forcing in transmission, and precipitate infection cycles. In the literature of (Anderson and May, 1991), a more disease – specific details such as, the latent period, the vaccinated population, chronic and acute stages of infection were included in their model.

The refinement of compartmental models to include heterogeneity of the population into the model has been of great help. This is done by distinguishing between population subgroups with different behaviors.

Hethcote and Yorke (Heathcoat and Yorke, 1994), introduced heterogeneity in behavior into their model in their research on the spread of sexually transmitted diseases. Several compartmental models were proposed during HIV/AIDS pandemic, which described population heterogeneity in sexual activity levels, (Koopman, 1998).These models were used to assess the effects of intervention on the spread of HIV/AIDS, and sexually transmitted disease on a whole.

Diekmann (Diekmann, 1990) developed the theory of finding and computing the reproduction number in heterogeneous populations.

Age structure is a type of compartmental model with several compartments of individuals ranging from one compartment to another, according to aging rate.

2.9.2 MODELS FOR VECTOR-BORN INFECTIONS

(Ronald Ross, 1911), introduced the idea of mass action in continuous time in his study of the transmission of malaria. Ross' work qualifies him as the founding father of modern epidemic theory. It was partly under his influence that Anderson McKendrick started his own studies into the mathematical modeling of epidemic phenomena, at first also in the context of malaria and other tropical infections. The works of Kermack and McKendrick are regarded as the foundation upon which much of modern theory rests (Anderson and May, 1991).

One of the distinguishing characteristics of malaria is that the protozoan parasite is indirectly transmitted between humans by mosquitoes. Several important human infections depend on similar vectors for their transmission. For modeling this introduces a new problem, the need to include the population dynamics of the vector

2.9.2.1 MODELING MALARIA

A simple model that captures the essential elements of malaria epidemiology is

$$\frac{dp}{dt} = uv\frac{M}{N}q(1-p) - \gamma p$$

$$\frac{dq}{dt} = utp(1-q) - uq$$

Where p and q are the functions of infected humans and mosquitoes respectively; M/N is the number of (female) mosquitoes per human host in an infected free steady state; u is the per capita biting rate of mosquitoes on humans; v is the probability that a bite by an infectious mosquito transmits the parasite; t is the probability that a bite of an infected human by a susceptible mosquito results in transmission of the parasite to the mosquito; γ is the rate at which

humans recover from infection; and μ is the per capita death rate of mosquitoes. The basic reproduction number for this model is

$$R_0 = \frac{M}{N}\frac{u^2vt}{\gamma\mu}$$

This can be define as the expected time for which a typical infected human remains infectious$(1/\gamma)$, multiplied by the expected number of mosquitoes to which the parasite will be transmitted (ut), multiplied by the expected life-span of a mosquito $(1/\mu)$, multiplied by the number of mosquitoes per host (M/N), multiplied by the expected number of humans to which a mosquito will transmit the parasite (uv). Campaigns for Eradication have been aimed at controlling the mosquito population strongly enough to achieve $R_0 < 1$, that is because the threshold valve $R_0 = 1$ defines a threshold for M/N, the ratio of mosquitoes to humans.

2.9.3 MODELS FOR PARASITE POPULATIONS

The tropical helminth infections served as the framework of epidemic theory. Early work by Kostitzin in 1934 was followed thirty years later by Macdonald's study of schistosomiasis and a flourishing of activity in the seventies and eighties(Scott and Smith,1994).

A major difference between microparasite and macroparasite is that the former reproduce rapidly within the host, whereas the latter reproduce by releasing offspring into the environment, some of which eventually complete a life-cycle, becoming infective stages, and infect a new host. Hence, for infections caused by parasitic helminths the compartmental models that classify a host as susceptible, infectious, etc. are inappropriate, and a model that allows multiple infections in a single host is required. Again, the notion that the population of susceptible diminishes during the course of an epidemic does not necessarily hold, differential equation models no longer have a negative feedback mechanism that is automatically incorporated, and careful attention must be

paid to the mechanisms that regulate the parasite population. Early models for parasites of wild animals included increased mortality of the host due to parasite infection; therefore heavily parasitized hosts had a shorter life expectancy, and upon dying removed large numbers of parasites from the system. For many helminth infections of humans this would not be the case, and cognizance must be taken of regulatory mechanisms such as acquired immunity (Diekmann and Heesterbeek, 2000).

In situations where an individual's immunity to infection increases with frequent reinfection, it is not always clear how this should be modeled mathematically. Currently the word immuno-epidemiology is used to signify an area of modeling that attempts to link immunological processes within individual hosts with epidemiological processes of transmission between hosts. Given the implications that this interaction between immunity and epidemiology (and increasingly with evolution) has for control strategies this area is likely to see much activity by epidemic modelers in the near future (Grenfell and Dobson, 1995).

2.9.3.1 THE POPULATION DYNAMICS OF MACROPARASITES

A simple model for the dynamics of a population of parasitic helminthes in a host population of constant size is given by

$$\frac{dp}{dt} = \mu(Q(P) - 1)P$$

Where P is the mean number of parasites per host, μ is the rate of loss of parasites from the system and $Q(P)$ is the ratio of parasite transmission rate to loss rate. This model is applicable in a situation where host immunity is a fraction of current mean parasite burden. The number Q (0) is the basic reproduction number for the parasite population. It may be defined as the expected

number of offspring of a typical parasite that reaches reproductive maturity, in a completely susceptible host population. Hence, whereas for microparasites the reproduction number is defined in terms of secondary infections of hosts, for macroparasites it is defined in terms of the parasite population dynamics (Grenfell and Dobson, 1995).

2.9.4 MODEL WITH STRUCTURE

The infection that sparked off a tremendous increase in epidemic modeling activity in the 1980s was HIV.This has helped brought more realistic models of different infections of humans and animals for the past ten years. The progress of the whole area of epidemic modeling is no longer attached to specific classes of infections as it was in the early days. There has been much progress, not only on the applied front but also mathematical advances necessary to cope with the more complex models that aim to take relevant heterogeneity in the population into account.

The transmission of childhood infections depends upon the age-structure of the population, with greater contact between those in the same classroom. Models of sexually transmitted infections call for the incorporation of much structure, including age-structure and groups with differences in infectivity or susceptibility (Mollison, 1996). The contact structure of these models must take account of discrete characteristics such as sex, sexual preferences and sexual activity. Two complications are particularly important: varying infectivity as a function of time elapsed since infection and the implications of long lasting partnerships. The first complication is relevant to almost all infections; the second is related to sexual transmission. One of the key notions to come out of HIV modeling is that of a core-group of infected. This is a small group that is very active in making contacts and can keep the epidemic going in a much larger group where the internal contacts alone cannot sustain it (Isham and Medley, 1996).

2.9.4.1 ADDING MORE CLASSES

Consider an *SIR* model for the transmission of an infection within a population that may be divided into n classes, for which the contact rate within classes may be different to those between classes. The classes may be based on, for example, sex or sexual orientation, school attended or college year. Neglecting mortality within the population at risk, the model equations for the densities of the susceptible (S_i) and infectious (I_i) populations are

$$\frac{dS_i}{dt} = A_i - (\mu_i + \beta \sum_{j=1}^{n} C_{ij} I_j) S_i$$

$$\frac{dI_i}{dt} = \beta S_i \sum_{j=1}^{n} C_{ij} I_j - (\mu_i + \gamma) I_i$$

For $i = 1 \ldots n$. A_i and μ_i are the recruitment rates into class i, and the rates at which individuals leave i respectively.

2.9.5 MATHEMATICAL MODELING OF HIV

Mathematical models have served as an aid to understanding the transmission dynamics of immunodeficiency syndrome (AIDS).Ever since the discovery of HIV as the primary virus associated with AIDS, several mathematical models have been constructed both deterministic and stochastic, to determine the rate of HIV progression to AIDS, optimal drug regimes, and the effect of the intracellular latency period on progression to disease (Murray, 2003).

Deterministic models assume large population size such that stochastic effects can be neglected. These models are applicable to the later stages of the process when the population is large (Shonkwiler and Herod, 2009).A list of work that has been done in this area are (Mclean and Nowak, 1992), (Frost and Mclean, 1994), (Kirschner and Webb, 1997), (Wein, 1998).

Stochastic models account for the early events in the disease when there are few infected cells and a small number of viruses (Murray, 2003). (Nowak, 1996), used stochastic model to look for the effects of variability among viral strains.

The best mathematical model of HIV so far has been the work of (Ho,1995).Ho ,used differential equations ,together with some patient data, and proposed a treatment strategy for the public health.However,this treatment strategy is no more in used, because of its failure in controlling and eradicating the disease, and its effects on many antiretroviral drugs.

HIV/AIDS modeling has been a controversial area since the complete understanding of the disease mechanism and its interaction with the immune system is lacking.

2.9.6 USE OF MODELING FOR PUBLIC HEALTH

Mathematical models have served as an aid to assess the effectiveness of vaccination strategies, to determine the best vaccination ages and target group and to estimate strategies in which infection can be eliminated from a population (Fergusion, 2003).

Mathematical modeling has also been of great help to the public health in planning response strategies to an epidemic outbreak such as the case of pandemic strain of influenza (Ferguson, 2006).Modeling also help in intervention measures of epidemic outbreak (Kretzschmar,2001).

However, it must be stated that the application of mathematical model to public health situation, requires an intensive focusing on a relevant data source, clinical and microbiological knowledge to make a decision about how to design an appropriate model.

CHAPTER 3

METHODOLOGY

3.1 Introduction

In this chapter, we will review the dynamics of ordinary differential equations and apply it to the deterministic SIR Epidemic model. Stochastic model will then be introduced immediately the deterministic is understood. Then we will illustrate some of the differences in the stochastic and the deterministic model formulation. We will also discuss the meaning and importance of the Basic Reproduction Number in respect to modeling of infectious disease and use it to investigate the qualitative dynamics of the deterministic model with solution paths and phase portraits.

Also, since our model is a two dimensional system, most of our discursion would be limited to two dimensional systems.

3.2 Ordinary Differential Equations

An equation of the form

$$\frac{dy}{dt} = f(t, y) \tag{3.1}$$

Where $f: R^2 \to R$ is a function of two or more variables and that the expression $\frac{dy}{dt}$ represents the derivative of y with respect to t is called ordinary differential equation (ODE). Any function $y = u(t)$ that satisfies $u'(t) = f(t, Q(t))$ is said to be the solution of the differential equation (3.1).The order of a differential equation is the order of the highest ordered derivative in the equation; thus equation (3.1) is a first order differential equation. Differential equations can also be of a higher order derivative such as

$$y^n = f(t, y, y^{|}, y^{||}, \dots\dots\dots, y^{(n-1)}) \tag{3.2}$$

The equation (3.11) is n^{th} order differential equation. The vector generalization of (3.1) where $y = (y_1\ y_2 \dots\dots\dots\dots\dots y_n)^T \in R^n$ and $f: R \times R^n \to R^n$ is given by

$$\left.\begin{aligned} y_1{}^{|} &= f_1(t, y_1, y_2, \dots\dots\dots y_n) \\ &\vdots \\ y_n{}^{|} &= f_n(t, y_1, y_2, \dots\dots\dots y_n \end{aligned}\right] \tag{3.3}$$

The system (3.2) is a first order system of differential equations and such equations are useful in the study of dynamical systems.

3.3 Eigenvalue

Let $A = [a_{ik}]$ be an $n \times n$ matrix. Consider the equation $Ax = \lambda x$, where λ is a scaler (a real or complex number) to be determined and x is a vector to be determined. Now for every λ a solution is $x = 0$. A scaler λ such that $(Ax = \lambda x)$ holds for some vector $x \neq 0$ is called an eigenvalue of A, and this vector is called an eigenvector of A corresponding to this eigenvalue λ.

Thus $Ax = \lambda x$

$$(Ax - \lambda I)x = 0$$

These are n linear algebraic equations in the n unknowns $x_1 \dots\dots\dots\dots x_n$ (the components of x).For these equations to have a solution$x \neq 0$, the determinant of the co-efficient matrix $A - \lambda I$ must be zero.

Let $A = \begin{pmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{pmatrix}$ $I = \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix}$

Then $(A - \lambda I)x = 0$

$$\Rightarrow \quad \begin{pmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{pmatrix} - \lambda \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix} \begin{pmatrix} x_1 \\ x_2 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \end{pmatrix}$$

$$\begin{pmatrix} a_{11} - \lambda & a_{12} \\ a_{21} & a_{22} - \lambda \end{pmatrix} \begin{pmatrix} x_1 \\ x_2 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \end{pmatrix}$$

$$\Rightarrow \quad (a_{11} - \lambda)x_1 + a_{12}x_{2=0}$$

$$a_{21}x_1 + (a_{22} - \lambda)x_2 = 0$$

Now $A - \lambda I$ is singular if and only if its determinant $\det(A - \lambda I)$, called the characteristics determinant of A is zero.

$$\det(A - \lambda I) = \begin{vmatrix} a_{11} - \lambda & a_{12} \\ a_{21} & a_{22-\lambda} \end{vmatrix}$$

$$= (a_{11} - \lambda)(a_{22} - \lambda) - a_{12}a_{21}$$

$\lambda^2 - (a_{11} + a_{22})\lambda + a_{11}a_{22} - a_{12}a_{21} = 0$, which is the characteristic equation of A.

Hence the characteristic equation is $\lambda^2 - (trace\ A)\lambda + detA = 0$. The solution of the characteristic equation are the eigenvalues λ_1 and λ_2 of A.

Eigenvalues determine the nature of the solution. If both eigenvalues λ_1 and $\lambda_2 < 0$,then the solution is stable, otherwise the solution is unstable.

Example 1.1

Given the system $y_1' = -4y_1 + 4y_2$

$$y_2' = -1.6y_1 - 3y_2$$

Since $y' = Ay = \begin{pmatrix} -4 & 4 \\ -1.6 & 1.2 \end{pmatrix} y$, then $= \begin{pmatrix} -4 & 4 \\ -1.6 & 1.2 \end{pmatrix}$.

Therefore the characteristics equation $\lambda^2 - (trace\ A)\lambda + det\ A = 0$ is given by

$$\lambda^2 - (-2.8)\lambda + 1.6 = 0.$$

Hence the eigenvalues of A are $\lambda_1 = -0.8$ and $\lambda_2 = -2$.

3.4 Stability of Eigenvalues

Consider a two-dimensional system:

$$\dot{x} = p(x, y),$$

$$\dot{y} = q(x, y),$$

and suppose $(\bar{x},\ \bar{y})$ is a steady state, then $p(\bar{x}, \bar{y}) = 0$ and $q(\bar{x}, \bar{y}) = 0$. To determine whether the steady state is stable or unstable, a small perturbation from the steady state is considered by letting

$$x = \bar{x} + f$$

$$y = \bar{y} + g$$

Where f and g are considered to be small enough. To determine whether f and g move towards the steady state or away from the steady state, we let

$f = \dot{x}$, since $\bar{x}$ is a constant. But $\dot{x} = p(x, y)$, hence

$f = p(x, y)$, substituting x and y gives

$$f = p(\bar{x} + f, \bar{y} + g)$$

By Taylor expansion,

$$= p(\bar{x}, \bar{y}) + \frac{dp}{dx}(\bar{x}, \bar{y})f + \frac{dp}{dy}(\bar{x}, \bar{y})g \ldots\ldots\ldots\ldots\ldots$$

Since $(\bar{x}, \bar{y}) = 0$, it implies

$$\dot{f} = \frac{dp}{dx}(\bar{x}, \bar{y})f + \frac{dp}{dy}(\bar{x}, \bar{y})g$$

Similarly

$$\dot{g} = \frac{dq}{dx}(\bar{x}, \bar{y})f + \frac{dq}{dy}(\bar{x}, \bar{y})g$$

Since f and g are assumed to be small, higher terms of f^2, g^2, fg can be neglected. Hence the linearized system of the equation of the perturbations f and g is

$$\begin{pmatrix} \dot{f} \\ \dot{g} \end{pmatrix} = \begin{pmatrix} \frac{dp}{dx}(\bar{x}, \bar{y}) & \frac{dp}{dx}(\bar{x}, \bar{y}) \\ \frac{dq}{dx}(\bar{x}, \bar{y}) & \frac{dq}{dx}(\bar{x}, \bar{y}) \end{pmatrix} \begin{pmatrix} f \\ g \end{pmatrix}$$

This matrix is called the Jacobian matrix of the original system at the steady state $(\bar{x}, \bar{y})$. The linear system for f and g has a trivial steady state $(f, g) = (0,0)$. The Jacobian matrix needs to be calculated once for each nonlinear system. For each critical point of the system, we can compute the coefficient matrix of the linearized system about a given critical point and then use its eigenvalues to determine the stability of the original nonlinear system.

Example 1.2

Consider the system

$$\dot{x} = -4y + 2xy - 8$$

$$\dot{y} = 4y^2 - x^2$$

The critical points are $(-2,-1)$ and $(4,2)$.The Jacobian matrix is

$$J = \begin{bmatrix} 2y & -4+2x \\ -2x & 8y \end{bmatrix}$$

At $(-2,-1)$, the linearized system has a coefficient matrix

$$A = \begin{bmatrix} -2 & -8 \\ 4 & -8 \end{bmatrix}$$

The characteristic equation $\lambda^2 - (traceA)\lambda + detA = 0$ is given by

$$\lambda^2 + 10\lambda + 48 = 0$$

Eigenvalues are $\lambda_1 = -5 + 4.7958$ and $\lambda_2 = -5 - 4.7958$

At $(4,2)$, the linearized system has a coefficient matrix

$$A = \begin{bmatrix} 4 & 4 \\ -8 & 16 \end{bmatrix}$$

The characteristic equation $\lambda^2 - (traceA)\lambda + detA = 0$ is given by

$$\lambda^2 - 20\lambda + 96 = 0$$

Eigenvalues are $\lambda_1 = 12$ and $\lambda_2 = 8$

3.5 The Phase Plane (Phase Portrait)

Consider a system of linear differential equation $y^{|} = Ay$. Its phase portrait is a representative set of its solutions, plotted as a parametric curves (where t is the parameter) on the Cartesian plane tracing the path of each particular solution $(x, y) = \big(x_1(t), x_2(t)\big), -\infty < t < \infty$. Phase portrait is a graphical representation of the nature of the solution of a given system of differential equation. The Cartesian plane where the phase portrait resides is called the phase plane. The parametric curves traced by the solutions are called trajectories.(see [10] for more on Phase portrait).

3.6 The critical point

An equilibrium solution of the system $y^{|} = Ay$ is the point $(y_1, y_{2)}$ where $y^{|} = 0$, that is, where $y_1{}^{|} = 0 = y_2{}^{|}$. An equilibrium solution is a constant solution of the system, and is usually called a critical point. For a linear system $y^{|} = Ay$, an equilibrium solution occurs at each solution of the system (of homogenous equation) $Ay = 0$. The system has exactly one solution, located at the origin, if $\det(A) \neq 0$. If $\det(A) = 0$, then the system has many infinite solutions. (See [10] for more on critical point).

3.6.1 Types of Critical Point

There are five types of critical points depending on the geometric shape of the trajectories near them. These are

- Improper nodes
- Proper nodes
- Saddle Points

- Centers
- Spiral Points

3.6.2 Improper Nodes

An improper node is a critical point p_0 at which all the trajectories, except for two of them, have the same limiting direction of the tangent. The two exceptional trajectories also have a limiting direction of the tangent at p_0 which, however, is different. Improper nodes are asymptotically stable if both eigenvalues are negative. It is unstable if the eigenvalues are positive.

Example 1.3

Consider the system $x^{|} = -3x + y$

$$y^{|} = x - 3y$$

Since $y^{|} = Ay = \begin{pmatrix} -3 & 1 \\ 1 & -3 \end{pmatrix} y$, then $A = \begin{pmatrix} -3 & 1 \\ 1 & -3 \end{pmatrix}$.

The characteristic equation $\lambda^2 - (traceA)\lambda + detA = 0$ is given by

$$\lambda^2 + 6\lambda + 8 = 0$$

The eigenvalues are $\lambda_1 = -2$ and $\lambda_2 = -4$

Improper node occurs when there are repeated real eigenvalues, and one linearly independent eigenvector. The phase portrait of an improper node looks like that of a node. The trajectories of an improper node all diverge away from the critical point to an infinite distant when $\lambda > 0$.

When $\lambda < 0$, the trajectories all converge to the critical point. It is asymptotically stable if $\lambda < 0$, and unstable if $\lambda > 0$.

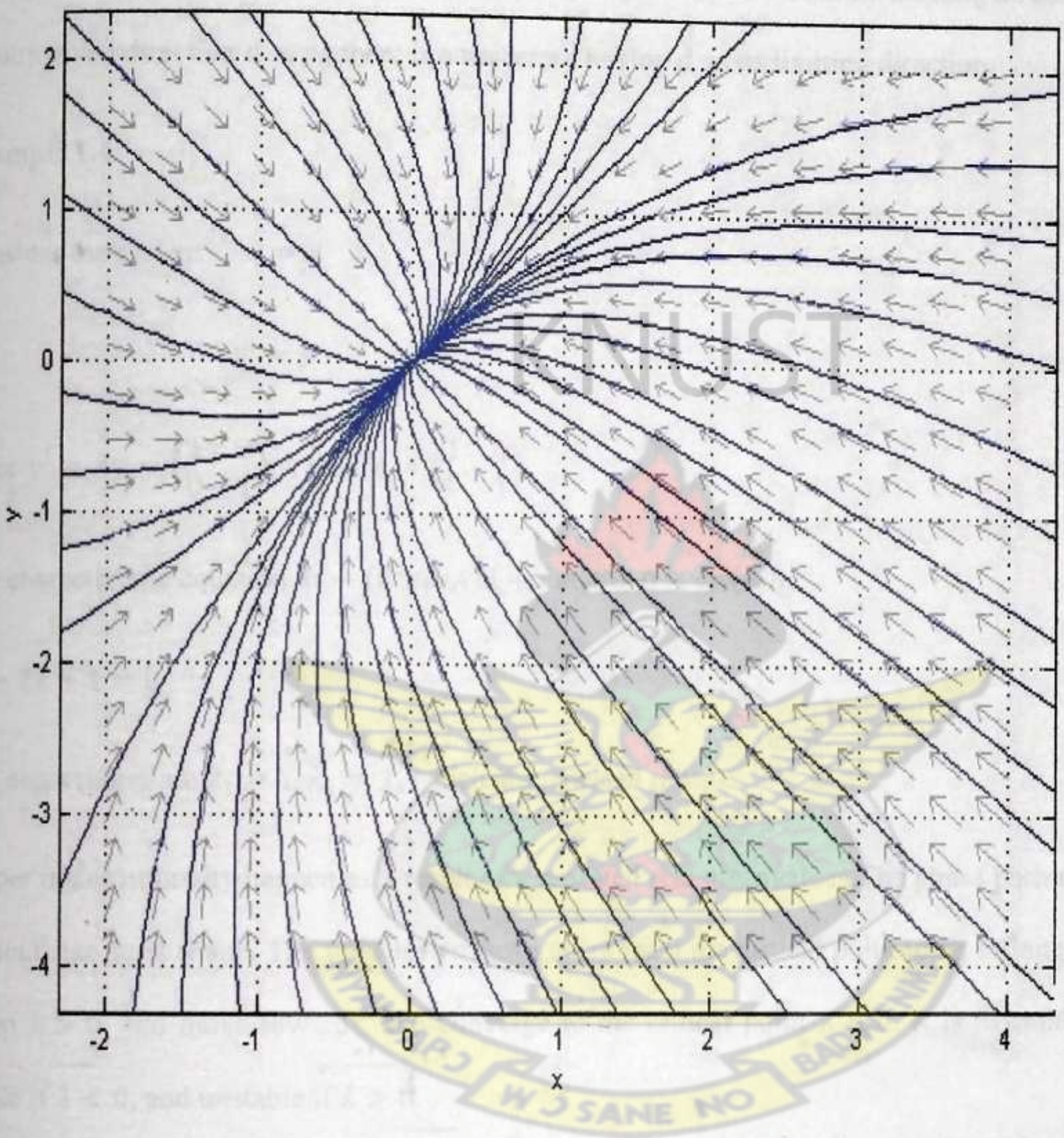

Figure 3.1. Phase Portraits of an Improper node generated using dfield8 and pplane8 from Matlab with the $x-axis$, $-2 \leq x \leq 4$ and the $y-axis$, $-4 \leq y \leq 2$ and the $x^{l} = -3x + y$ and $y^{l} = x - 3y$

3.6.3 Proper Node

A proper node is a critical point p_0 at which every trajectory has a definite limiting direction and for any given direction d at p_0 there is a trajectory having d as its limiting direction.

Example 1.4

Consider the system $x^{|} = x$

$$y^{|} = y$$

Since $y^{|} = Ay = \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix} y$, then $A = \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix}$

The characteristic equation $\lambda^2 - (traceA)\lambda + detA = 0$ is given by

$\lambda^2 - 2\lambda + 1 = 0$

The eigenvalues are $\lambda_1 = 1, \lambda_2 = 1$, which are repeated root.

Proper nodes normally happen as a result of a repeated real eigenvalues.The phase portrait has a distinct star-burst shape. The trajectories move away from the critical point to an infinite distant when $\lambda > 0$, and move towards, and converge to the critical point $\lambda < 0$. It is asymptotically stable if $\lambda < 0$, and unstable if $\lambda > 0$.

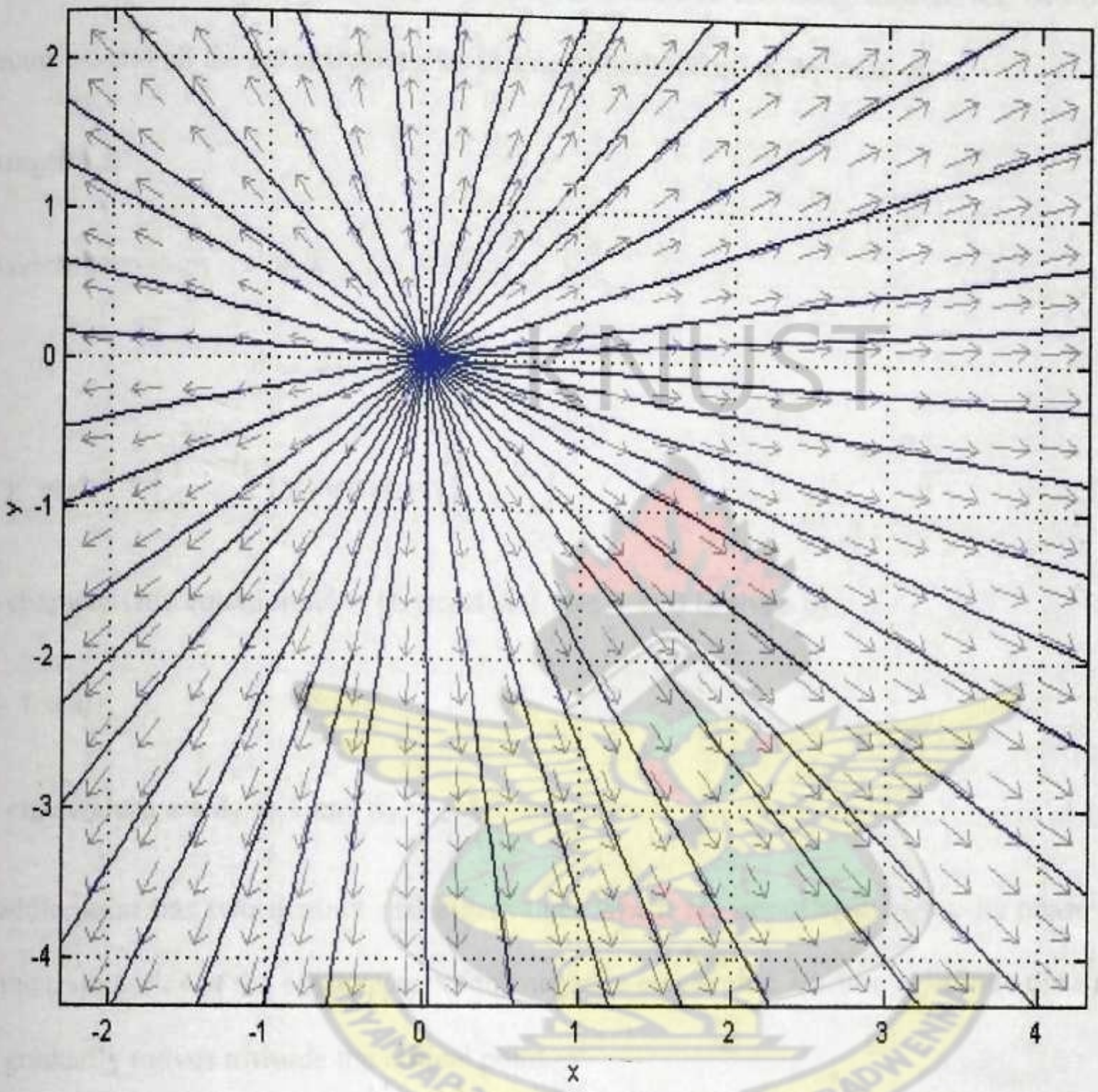

Figure 3.2. Phase Portraits of a Proper node generated using dfield8 and pplane8 from Matlab with the $x-axis$, $-2 \leq x \leq 4$ and the $y-axis$, $-4 \leq y \leq 2$ and the $x^{|} = x$ and $y^{|} = y$

3.6.4 Saddle Point

A saddle point is a critical point p_0 at which there are two incoming trajectories, two outgoing trajectories, and all the other trajectories in a neighborhood of p_0 by pass p_0.

Example 1.5

Consider the system $x^{|} = x$

$$y^{|} = -y$$

But $y^{|} = Ay = \begin{pmatrix} 1 & 0 \\ 0 & -1 \end{pmatrix} y$,then $A = \begin{pmatrix} 1 & 0 \\ 0 & -1 \end{pmatrix}$

The characteristic equation $\lambda^2 - (traceA)\lambda + det\ A = 0$ is given by

$\lambda^2 - 1 = 0$

The eigenvalues are $\lambda_1 = 1$ and $\lambda_2 = -1$

A saddle point has two distinct real eigenvalues which are opposite in signs. Its phase portrait has the trajectories of the eigenvector of the negative eigenvalue, starting at infinite distant away, and gradually moves towards the critical point.

The trajectories of the eigenvector of the positive eigenvalue also start at the critical point, and gradually move away from the point. All other trajectory starts a distant from the critical point, and moves toward the critical point, but never converges, since its direction is diverted.

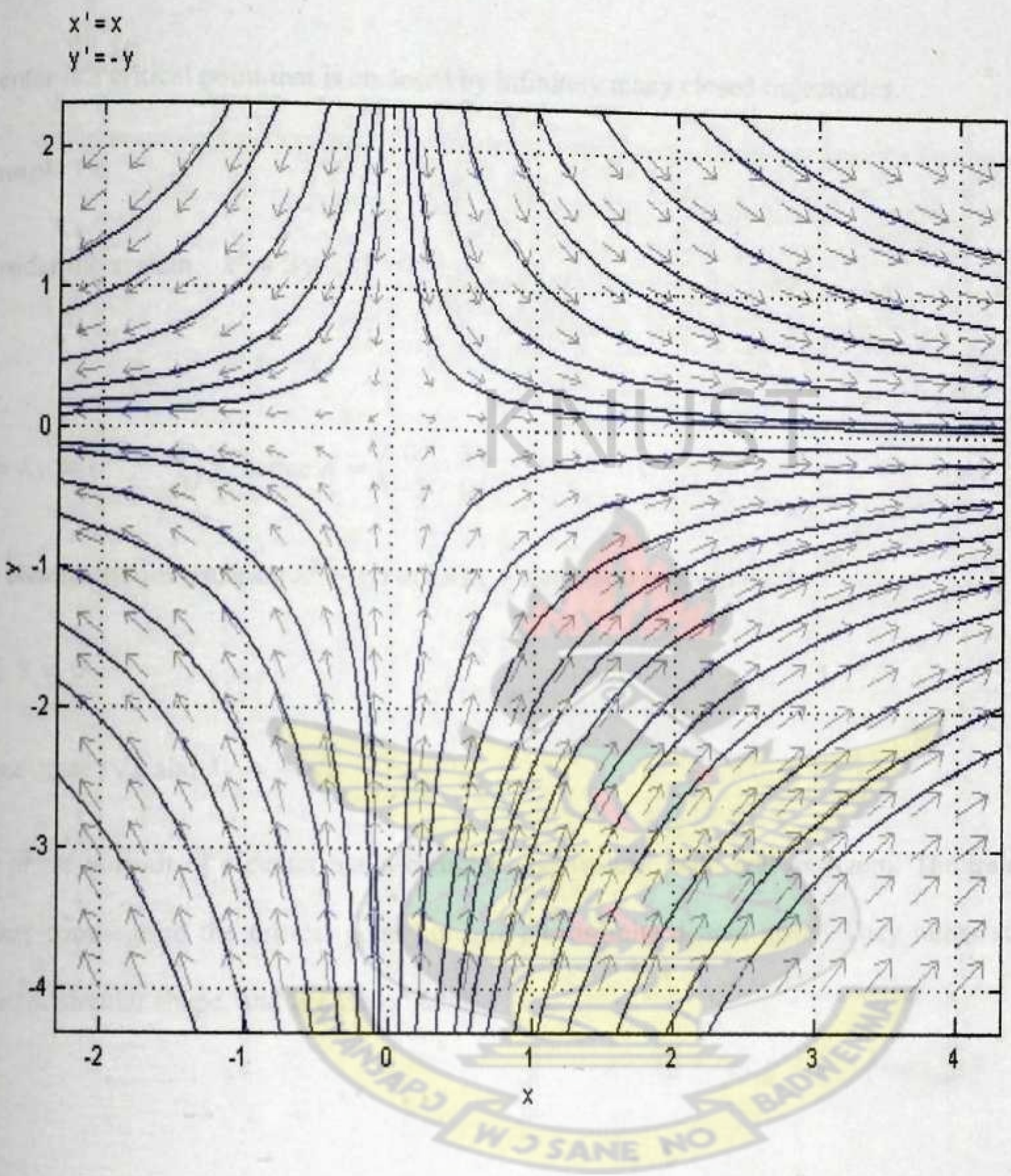

Figure 3.3. Phase Portraits of a Saddle Point generated using dfield8 and pplane8 from Matlab with the ~~$x-axis$~~, $-2 \leq x \leq 4$ and the $y-axis$, $-4 \leq y \leq 2$ and the $x^{l} = x$ and $y^{l} = -y$

3.6.5 Center

A center is a critical point that is enclosed by infinitely many closed trajectories.

Example 1.6

Consider the system $x^{|} = 3y$

$$y^{|} = -x$$

$y^{|} = Ay = \begin{pmatrix} 0 & 3 \\ -1 & 0 \end{pmatrix} y$, hence $A = \begin{pmatrix} 0 & 3 \\ -1 & 0 \end{pmatrix}$

The characteristics equation $\lambda^2 - (traceA)\lambda + detA = 0$ is given by

$\lambda^2 + 3 = 0$

Hence $\lambda_1 = i\sqrt{3}$ and $\lambda_2 = -i\sqrt{3}$

The phase portrait of a center has a complex eigenvalues, with real part zero. The trajectories neither converge to the critical point nor move to infinite distant away. They rather stay in a constant circular shape, and is always stable.

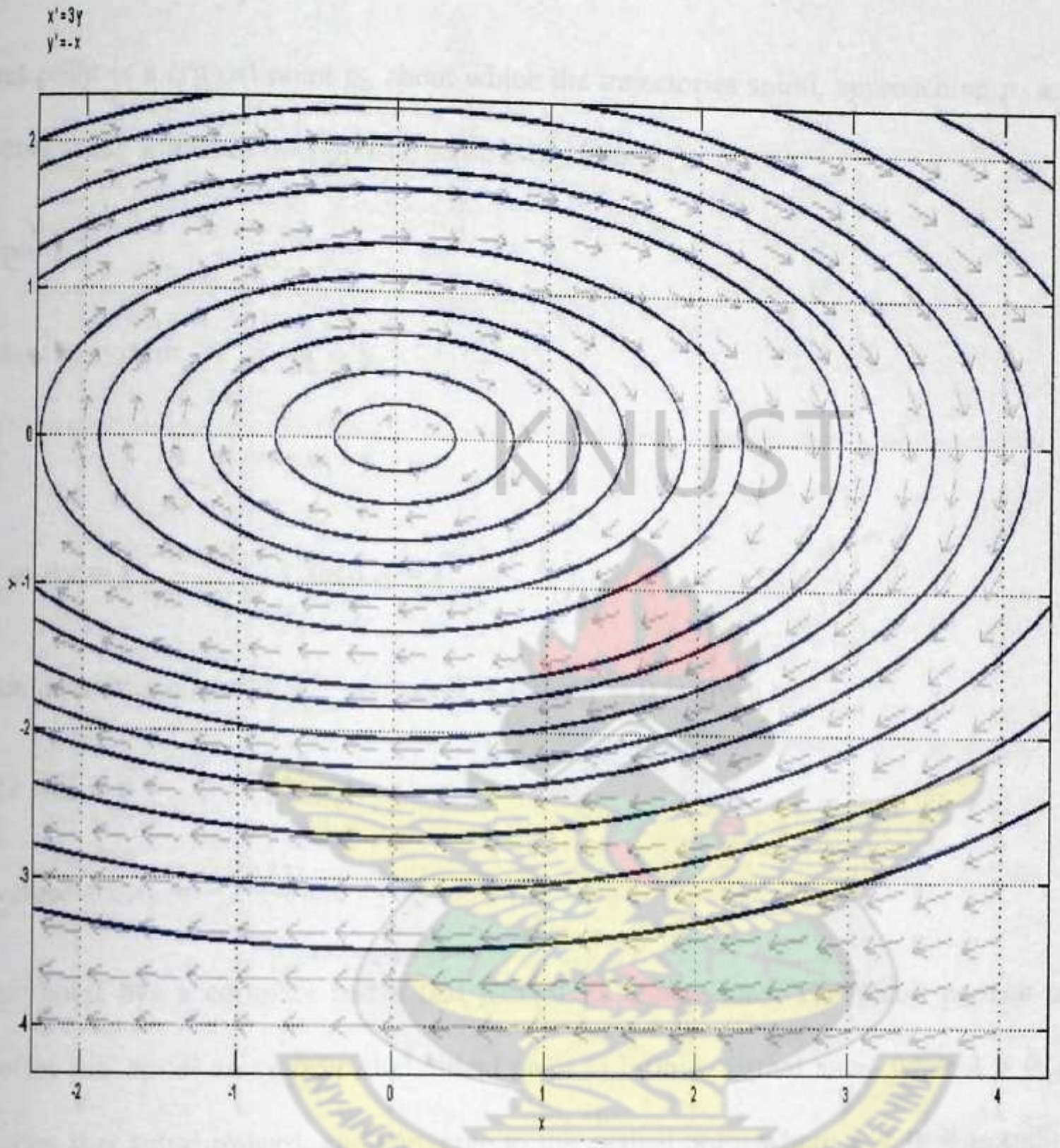

Figure 3.4. Phase Portraits of a Center generated using dfield8 and pplane8 from Matlab with the $x-axis, -2 \leq x \leq 4$ and the $y-axis, -4 \leq y \leq 2$ and the $x^{l} = 3y$ and $y^{l} = -x$

3.6.6 Spiral Point

A spiral point is a critical point p_0 about which the trajectories spiral, approaching p_0 as $t \to \infty$ (or tracing these spirals in the opposite sense away from p_0).

Example 1.7

Consider the system $x^{|} = -x + y$

$$y^{|} = -x - y$$

But $y^{|} = Ay = \begin{pmatrix} -1 & 1 \\ -1 & -1 \end{pmatrix} y$, then $A = \begin{pmatrix} -1 & 1 \\ -1 & -1 \end{pmatrix}$

The characteristics equation $\lambda^2 - (traceA)\lambda + detA = 0$ is given by

$\lambda^2 + 2\lambda + 2 = 0$

Eigenvalues are $\lambda_1 = -1 + i$ and $\lambda_2 = -1 - i$

A spiral point has a complex and a real part of its eigenvalues. The phase portrait shows a trajectories that spiral away from the critical point to infinite distant away when $\lambda > 0$, and the trajectories that spiral toward, and converge to the critical point where $\lambda < 0$. It is stable if the eigenvalues have positive real part, and asymptotically stable if the eigenvalues have negative real part.

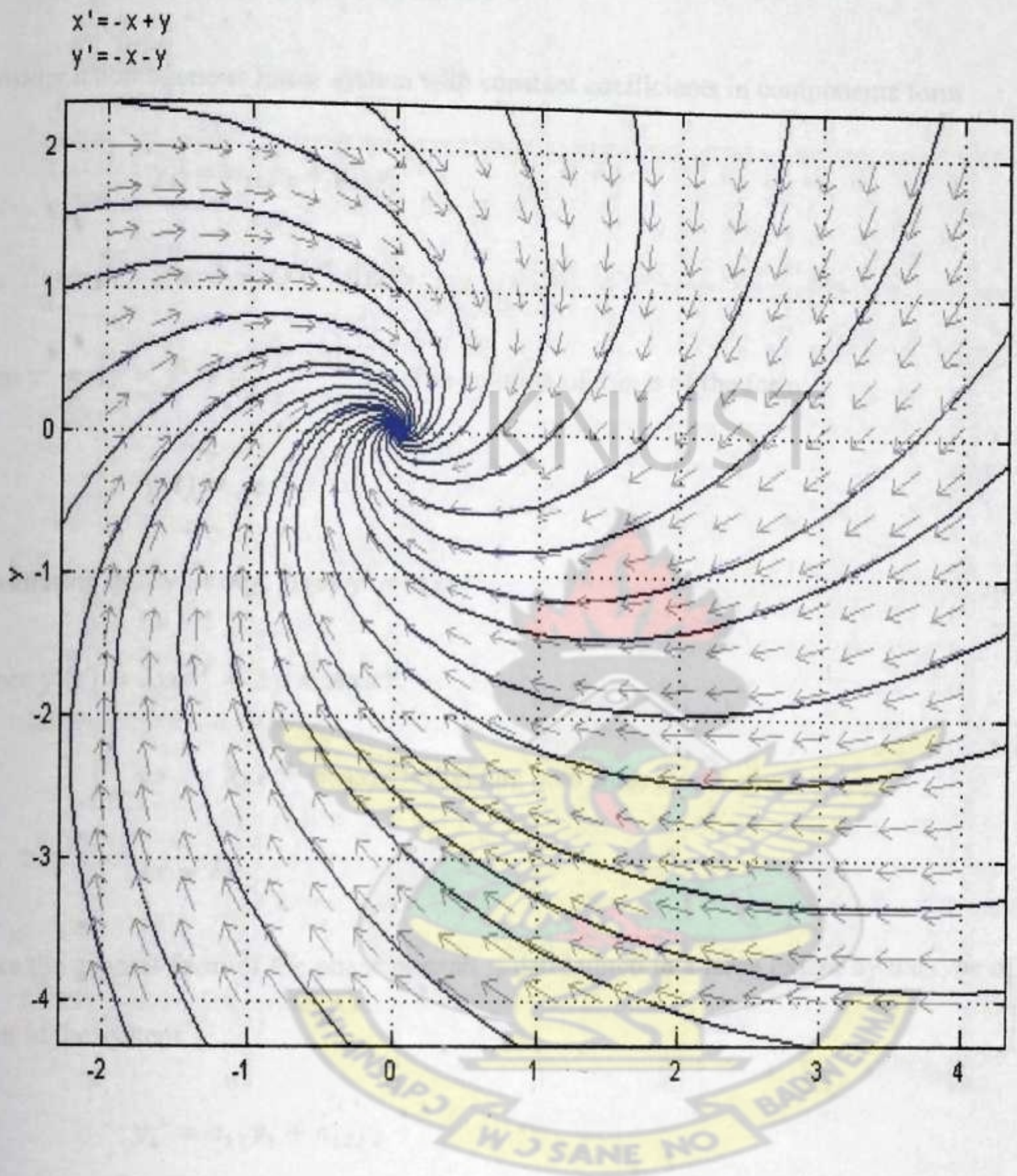

Figure 3.5. Phase Portraits of a Spiral Point generated using dfield8 and pplane8 from Matlab with the $x-axis,\ -2 \leq x \leq 4$ and the $y-axis,\ -4 \leq y \leq 2$ and the $x^{l} = -x + y$ and $y^{l} = -x - y$

3.7 Criteria for Critical points stability

Consider a homogenous linear system with constant coefficients in components form

$$y_1{}' = a_{11}y_1 + a_{12}y_2$$

$$y_2{}' = a_{21}y_1 + a_{22}y_2$$

Then $y' = Ay = y' = \begin{pmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{pmatrix} y$ .The solution of this is of the form

$$y(t) = xe^{\lambda t}$$

Substituting into $y' = Ay$, gives $y' = Axe^{\lambda t}$.

Hence $y'(t) = \lambda xe^{\lambda t} = Ay = Axe^{\lambda t}$

$\Rightarrow$ $\lambda xe^{\lambda t} = Axe^{\lambda t}$, dividing both sides by $e^{\lambda t}$ gives

$$Ax = \lambda x$$

Since the general form of the phase portrait is determined to a large extent by the type of critical point of the system

$$y_1{}' = a_{11}y_1 + a_{12}y_2$$

$$y_2{}' = a_{21}y_1 + a_{22}y_2$$

At the point where $\frac{dy_2}{dy_1}$ becomes undetermined, thus $^0/_0$.

$$\Rightarrow \quad \frac{dy_2}{dy_1} = \frac{y_2{}'dt}{y_1{}'dt} = \frac{a_{21}y_1 + a_{22}y_2}{a_{11}y_1 + a_{12}y_2}$$

Since critical points are related to the eigenvalues, then the characteristic equation for $\lambda = \lambda_1$ and λ_2 are

$$\det(A - \lambda I) = \begin{vmatrix} a_{11} - \lambda & a_{12} \\ a_{21} & a_{22} - \lambda \end{vmatrix} = \lambda^2 - (a_{11} + a_{22})\lambda + detA = 0.$$

This gives quadratic equation $\lambda^2 - u\lambda + v = 0$ with coefficients u, v and discriminant Δ given by

$u = (a_{11} + a_{22})$ →Trace of A

$v = \det A = a_{11}a_{22} - a_{12}a_{21}$

$\Delta = u^2 - 4v$

The solution of the characteristic equation is given by

$$\lambda_1 = \frac{1}{2}(u + \sqrt{\Delta}) \text{ and } \lambda_2 = \frac{1}{2}(u - \sqrt{\Delta})$$

The product representation of the equation is given by

$$\lambda^2 - u\lambda + v = \lambda^2 - (\lambda_1 + \lambda_2)\lambda + \lambda_1\lambda_2$$

Hence u and v are the sum and product of the eigenvalues. (see [10] for more on critical point stability).

$u = \lambda_1 + \lambda_2$ $\quad v = \lambda_1\lambda_2$ $\quad \Delta = (\lambda_1 - \lambda_2)^2$

Table 3.1 Eigenvalue criteria for Critical Point

Name	$u = \lambda_{1+}\lambda_2$ Trace of A	$v = \lambda_1\lambda_2$ Det of A	$\Delta = (\lambda_1 - \lambda_2)^2$	Comments on λ_1, λ_2
Node		$v > 0$	$\Delta \geq 0$	Real, same sign
Saddle Point		$v < 0$		Real, opposite sign
Center	$u = 0$	$v > 0$		Pure imaginary
Spiral Point	$u \neq 0$		$\Delta < 0$	Complex,immaginary

3.8 Stability

Critical points may also be classified in terms of their stability. Stability means, that a small disturbance of a system changes the behavior of the system only slightly at all future times t. consider the system

$$y_1' = a_{11}y_1 + a_{12}y_2$$

$$y_2' = a_{21}y_1 + a_{22}y_2$$

A critical point p_0 of the system is called stable if all trajectories of the system that are close to p_0 remain close to p_0 at all future times(See [10], for more on stability).

Table 3.2 Stability criteria for Critical point

Types of Stability	$u = \lambda_1 + \lambda_2$(Trace)	$det\ v = \lambda_1\lambda_2$
Stable & attractive	$u < 0$	$v > 0$
Stable	$u \leq 0$	$v > 0$
Unstable	$u > 0$	$v < 0$

- If $v = \lambda_1\lambda_2 > 0$, both eigenvalues are positive or both are negative or complex conjugates.
- If $u = \lambda_1 + \lambda_2 < 0$, both eigenvalues are negative or have a negative real part. Hence p_0 is stable and attractive.
- If $\Delta < 0$, the eigenvalus are complex conjugates, thus $\lambda_1 = b + i\beta$ and $\lambda_2 = b - i\beta$,and if $u = \lambda_1 + \lambda_2 < 0$,this gives a spiral point that is stable and attractive

3.9 The Deterministic Model

These are mathematical models which are without randomness or noise. They are usually represented in the form of a set of ordinary differential equations (ODE). They are normally robustics and with one set of initial values, the system will generate only one solution.

3.10 The Basic Reproduction Number

The Basic Reproduction Number or Ratio is one of the most useful threshold parameters which characterize mathematical problems concerning infectious diseases. It is often use in epidemiological models.

The basic reproduction number (R_0) is defined as the expected number of new infections from a single infected individual placed into a population of fully susceptible individuals .Thus R_o tells us about the initial spread of the disease.

If $R_o < 1$, then a single infected individual introduced into the population will die, without being not able to replace themselves by new infection. Conversely, if $R_o > 1$, there will be an epidemic.

For the case of a single infected compartment, R_o is simply the product of the infection rate and the mean duration of the infection. However, for more complicated models with several infected compartments, this parameter is established by investigating the stability of disease free equilibrium. The parameter provides significant insight into the transmission dynamics of a disease and can guide strategies to control its spread.

3.11 Deterministic SIR Epidemic Model

Consider a simple SIR model for HIV in a mixing homogeneous population which can be grouped into three distinct compartments of Susceptible (S), infective (I), and Removed (R).

The model does not consider demographic turnovers (birth and death), and all infections are assumed to end with recovery. The total size of the population is constant and is denoted by $N = S(t) + I(t) + R(t)$, where $S, I, R \geq 0$, because they represent the numbers of people.

Further we assume that;

- Encounters between infective and susceptible individuals occur at a rate proportional to their respective numbers in the population. Thus the rate of new infection is defined as βSI, where $\beta > 0$ is a parameter for infectivity
- The rate of removal of infective to the removed class is proportional to the number of infectives, thus γI where $\gamma > 0$ is a constant
- The incubation period is short enough to be negligible; that is a susceptible who contracts the disease is infective right away.

Hence

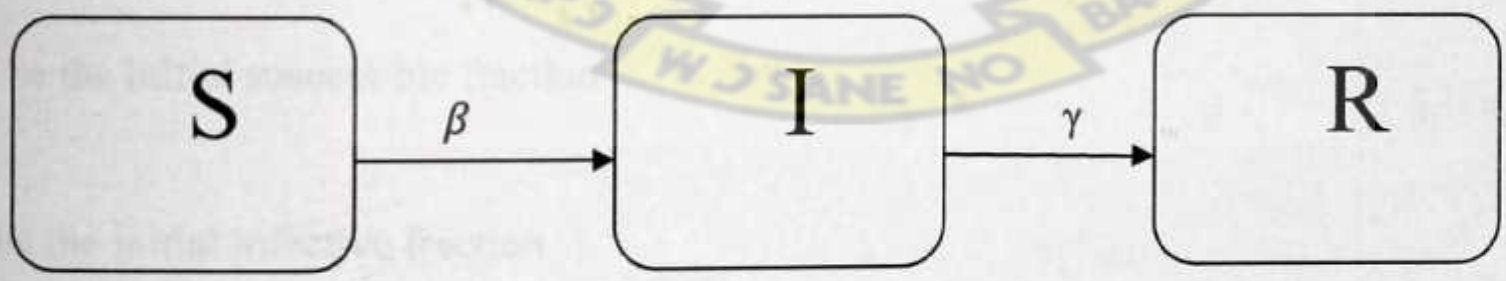

Figure 3.6 . A Schematic of system (3.1), Boxes represent compartments, and arrows indicate flux between the compartments.S is the susceptible,I is the infectives and R is the removeds,β is the infection rate,γ is the removal rate.

The differential equations describing this model are;

$$\frac{dS}{dt} = -\beta \frac{SI}{N} \qquad S(0) = S_0 \geq 0,$$

$$\frac{dI}{dt} = \beta \frac{SI}{N} - \gamma I \qquad I(0) = I_0 \geq 0, \tag{3.5}$$

$$\frac{dS}{dt} = \gamma I \qquad R(0) = R_0 \geq 0,$$

From $N = S + I + R$, dividing through by N gives

$$1 = \frac{S}{N} + \frac{I}{N} + \frac{R}{N}.$$

Let

$s = \frac{S}{N}$ be the susceptible fraction

$i = \frac{I}{N}$ be the infective fraction

$r = \frac{R}{N}$ be the removal fraction

Also let

$s_0 = \frac{S_0}{N}$ be the initial susceptible fraction

$i_0 = \frac{I_0}{N}$ be the initial infective fraction

$r_0 = \frac{R_0}{N}$ be the initial removal fraction

Since the total population N is constant, dividing system (3.5) by N gives

$$\frac{d}{dt}\left[\frac{S}{N}\right] = -\beta\frac{S}{N}\cdot\frac{I}{N}$$

$$\frac{d}{dt}\left[\frac{I}{N}\right] = \beta\frac{s}{N}\cdot\frac{I}{N} - \gamma\frac{I}{N} \qquad (3.6)$$

$$\frac{d}{dt}\left[\frac{R}{N}\right] = \gamma\cdot\frac{I}{N}$$

Substituting the fractional variables s, i, r into (3.6) gives

$$\frac{ds}{dt} = -\beta si \qquad s(0) = s_0 \geq 0$$

$$\frac{di}{dt} = \beta si - \gamma i \qquad i(0) = i_0 \geq 0 \qquad (3.7)$$

$$\frac{dr}{dt} = \gamma i \qquad r(0) = r_0 \geq 0$$

Since r affects neither s nor i, we neglect r.Hence the system reduces to two-dimensional equations;

$$\frac{ds}{dt} = -\beta si \qquad s(0) = s_0 \geq 0 \qquad (1)$$

$$\frac{di}{dt} = \beta si - \gamma i \qquad i(0) = i_0 \geq 0 \qquad (2) \qquad (3.8)$$

Dividing equation (2) of (3.8) by (1), we obtain

$$\frac{di}{ds} = \frac{\beta si - \gamma i}{-\beta si}, \qquad (3.9)$$

Simplifying (3.9) gives the equivalent equation

$$\frac{di}{dt} = -1 + \frac{\gamma}{\beta s}$$

But the reproduction number by definition is given by

$$\lambda = R_0 = \frac{\beta}{\gamma}$$

Hence $\frac{di}{ds} = -1 + \frac{1}{\lambda s}$ (3.10)

Separating (3.7) and solving with initial conditions gives

$$i(t) = -s(t) + i_0 + ln\frac{s(t)}{\lambda} - ln\frac{s_0}{\lambda} \quad (3.11)$$

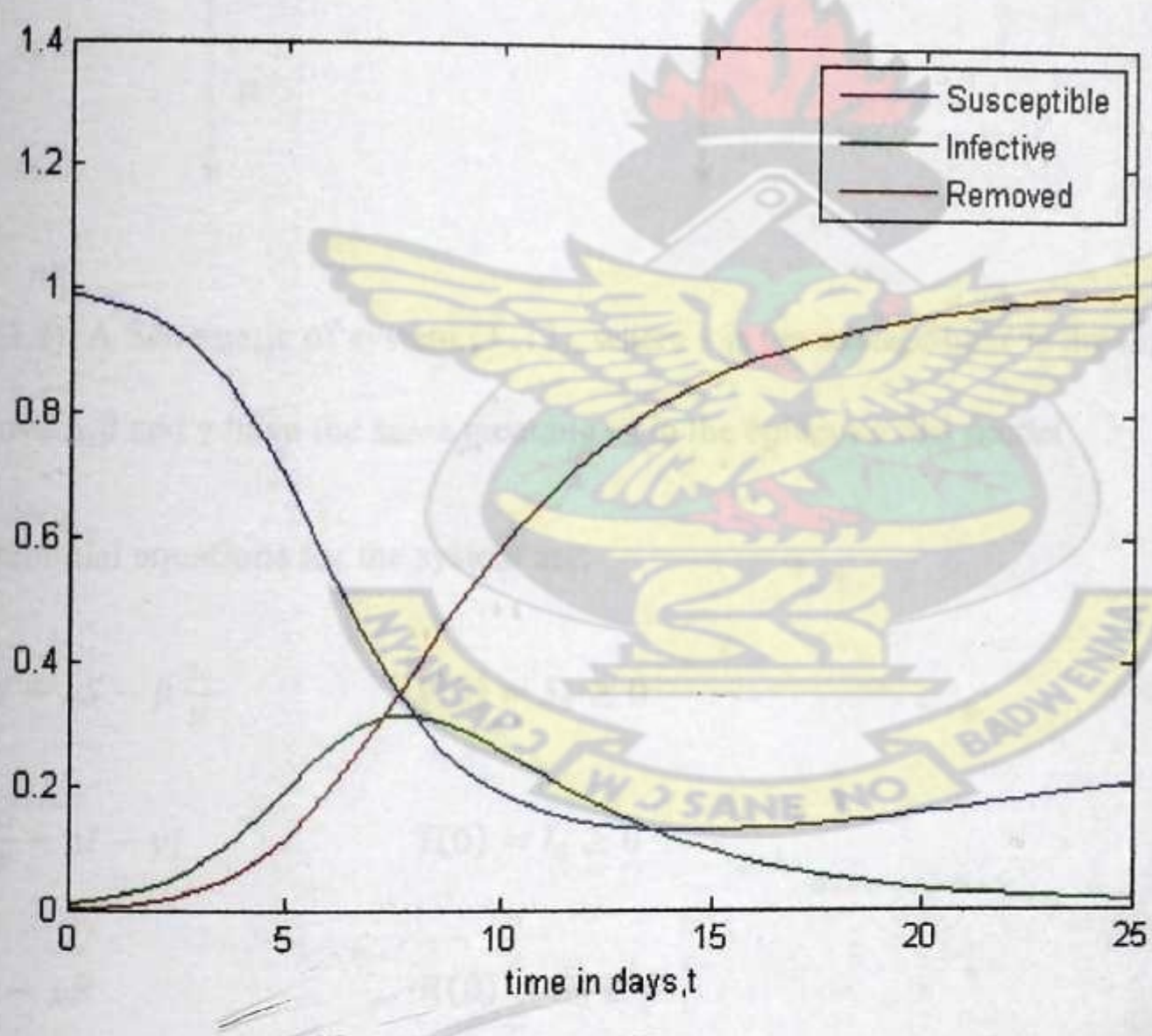

Figure (3.7): Phase portrait of Solution of the SIR epidemic model, $R_0 = 3$ with initial conditions $(s_0, i_0) = (0.99, 0.01)$

3.12 The Endemic SIR Model

Here we add the demographic turnovers (birth and death) and assume that the birth rate equal death rate so that the total size of the population will still remain constant.

Hence

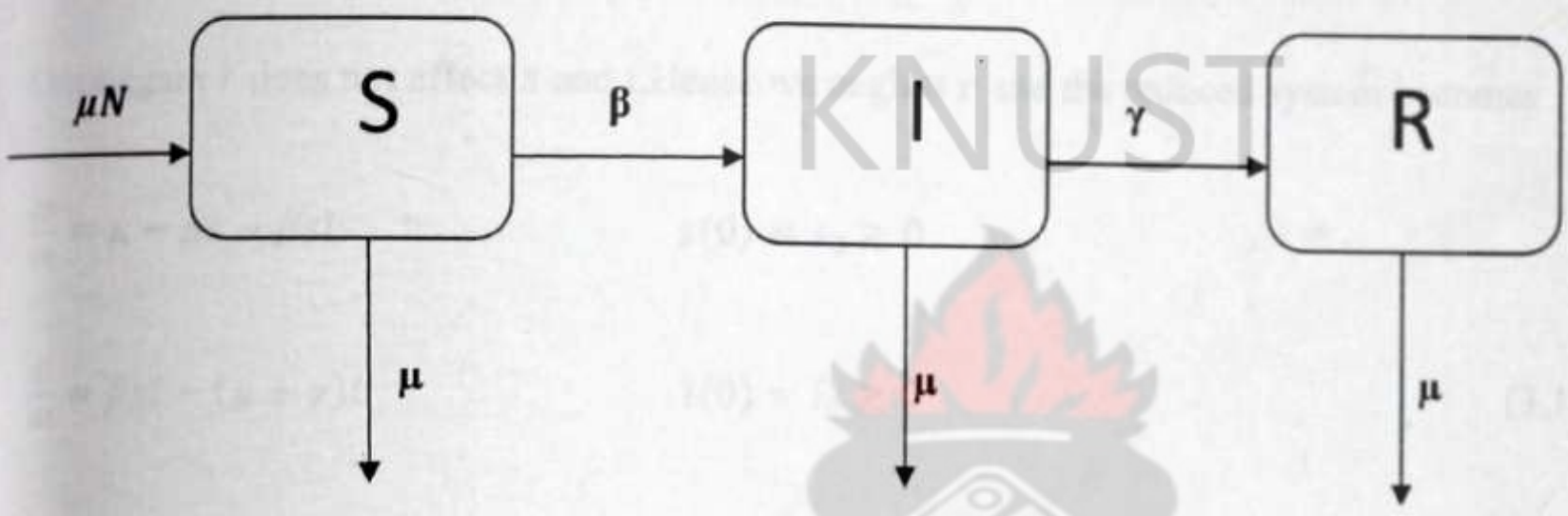

Figure (3.8). A Schematic of system (3 .13), where s is the susceptible,I is the infectives and R is the removeds.β and γ have the same meaning as in the epidemic SIR model.

The differential equations for the system are;

$$\frac{ds}{dt} = \mu N - \mu S - \beta \frac{SI}{N} \qquad S(0) = S_0 \geq 0$$

$$\frac{dI}{dt} = \beta \frac{SI}{N} - \mu I - \gamma I \qquad I(0) = I_0 \geq 0 \qquad (3.13)$$

$$\frac{dR}{dt} = \gamma I - \mu R \qquad R(0) = R_0 \geq 0$$

Where $N = S(t) + I(t) + R(t)$

A similar derivation as in section (3.13) gives the equivalent system of equations

$$\frac{ds}{dt} = \mu - \mu s - \beta si \qquad s(0) = s_0 \geq 0$$

$$\frac{di}{dt} = \beta si - (\mu + \gamma)i \qquad i(0) = i_0 \geq 0 \qquad (3.14)$$

$$\frac{dr}{dt} = \gamma i - \mu r \qquad r(0) = r_o \geq 0$$

Once again r does not affect s and i,Hence we neglect r and the reduced system becomes

$$\frac{ds}{dt} = \mu - \mu s - \beta si \qquad s(0) = s_0 \geq 0$$

$$\frac{di}{dt} = \beta si - (\mu + \gamma)i \qquad i(0) = i_0 \geq 0 \qquad (3.15)$$

With $r(t) = 1 - s(t) - i(t)$.

The reproduction number for this model is

$$R_0 = \frac{\beta}{\gamma + \mu}$$

If $R_0 > 1$ and $\gamma > 0$, then $\lim_{t\to\infty} I(t) = I_0 > 0$.

If $R_0 > 1$and $\gamma = 0$, then $\lim_{t\to\infty} I(t) = 0$.

There is an epidemic if $R_0 \cdot \frac{S(0)}{N} > 1$.

If $\lambda_0 \leq 1$,then $\lim_{t\to\infty} I(t) = 0$

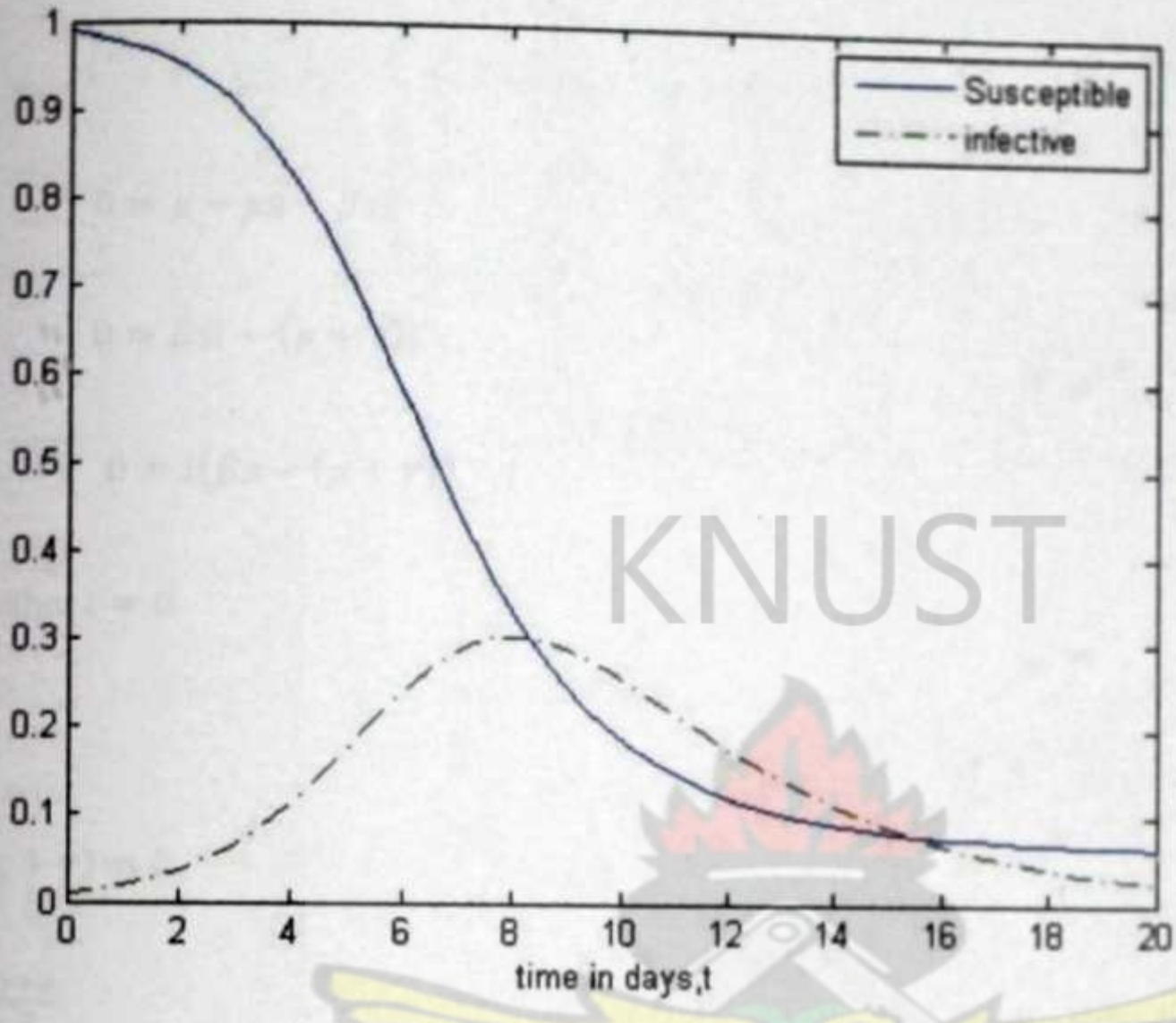

Figure (3.9): Phase portrait of Solution of the SIR epidemic model, $R_0 = 3$ with initial conditions $(s_0, i_0) = (0.99, 0.01)$

3.13 Equilibrium Points

The Stability of the model is found by evaluating the equilibrium points of the reduced system of the equations of (3.15).

These points are disease-free, where $i = 0$ and endemic, where $i \neq 0$.

To find these points, the right-hand side of equation (3.12) is equated to zero and the system is solved simultaneously for s and i.

Thus

$$0 = \mu - \mu s - \beta si \tag{3.16}$$

$$0 = \beta si - (\mu + \gamma)i \tag{3.17}$$

From (3.14) $0 = i(\beta s - (\mu + \gamma))$,

Hence either $i = 0$

or

$\beta s - (\mu + \gamma) = 0.$

$\Rightarrow s = \frac{\gamma+\mu}{\beta}$

But $\lambda = R_0 = \frac{\beta}{\mu+\gamma}$,

substituting gives $s = \frac{1}{\lambda}$.

Therefore equation (3.14) has solution $i = 0, s = \frac{1}{\lambda}$

Putting into equation (3.16) produces the equilibrium points $(s, i) = (1,0)$ and

$(s, i) = \left[\left(\frac{1}{\lambda}, \quad \frac{\mu(\lambda-1)}{\beta}\right)\right]$.

Clearly, the equilibrium point $(s, i) = (1,0)$ is the disease-free equilibrium since $i = 0$, and the point $(s, i) = \left(\frac{1}{\lambda}, \frac{\mu(\lambda-1)}{\beta}\right)$ is endemic equilibrium since $i = \frac{\mu(\lambda-1)}{\beta}$

3.14 Disease-free Equilibrium

The stability of the system at disease-free equilibrium is found by evaluating the jacobian of the system (3.12) at the equilibrium point $(s, i) = (1,0)$.

Let

$$V(s,i) = \mu - \mu s - \beta si$$

$$U(s,i) = \beta si - (\gamma + \mu)i$$

Hence the Jacobian of V and U is given by

$$J = \begin{bmatrix} \frac{dv}{ds} & \frac{dv}{di} \\ \frac{du}{ds} & \frac{du}{di} \end{bmatrix} = \begin{bmatrix} -\mu - \beta i & -\beta s \\ \beta i & \beta s - (\gamma + \mu) \end{bmatrix}$$

Therefore

$$J(s,i) = J(1,0) = \begin{bmatrix} -\mu & -\beta \\ 0 & \beta - (\gamma + \mu) \end{bmatrix}$$

Therefore by applying the characteristic equation formula for the (2×2) matrix

$$\lambda^2 - (traceA)\lambda + detA = 0$$

Since the Jacobian matrix is diagonal, it is clear that the eigenvalues are

$$\lambda_1 = -\mu \text{ and } \lambda_2 = \beta - (\gamma + \mu)$$

In order for the equilibrium point to be asymptotically stable, both eigenvalues must be negative.

It is clear that $\lambda_1 = -\mu$ is negative and that if $\lambda_2 = \beta - (\gamma + \mu) < 0$ then both eigenvalues are negative and the equilibrium point is asymptotically stable.

This means a small population of infectives introduced into the system would not cause a persistent infection and that the population would return to disease-free state after some time.

On the other hand, if $\beta - (\gamma + \mu) > 0$, then the equilibrium point is unstable and an introduction of infectives will result in a persistent infection. Hence there will be endemicity.

3.15 Endemic Equilibrium

For the equilibrium point $(s, i) = (\frac{1}{\lambda}, \frac{\mu(\lambda-1)}{\beta})$ the jacobian is given by

$$J(s,i) = \left(\frac{1}{\lambda}, \frac{\mu(\lambda-1)}{\beta}\right) = \begin{bmatrix} -\mu\lambda & \frac{-\beta}{\lambda} \\ \mu(\lambda-1) & 0 \end{bmatrix}$$

Then the characteristic equation is given by:

$$\lambda^2 - (-\mu\lambda) + \frac{\beta\mu(\lambda-1)}{\lambda} = 0.$$

Since the trace is less than zero and the determinant, $\frac{\beta\mu(\lambda-1)}{\lambda} > 0$,it satisfies that the endemic equilibrium is asymptotically stable (thus $\lambda > 1$ makes it stable).If $\lambda < 1$, it becomes unstable.

3.16 The Stochastic Model

These are mathematical models which have stochastic effect, and hence involve randomness. They can be formulated in terms of a stochastic process or stochastic differential equations (SDEs) or in terms of stochastic ordinary differential equations (SODEs). For stochastic model, with one set of initial values, the system may generate different solutions

3.17 Stochastic Process

A collection of random variables $\{X(t)|t > 0\}$ is called a stochastic process. Example of stochastic process is wiener process.

3.18 The Wiener Process $w(t)$

A real-valued stochastic process $w(t)$ is called a Brownian motion or wiener process if it satisfies the following properties.

- $w(t)$is continuous and $w(0) = 0$(with probability 1)
- For $0 \leq s < t \leq T$ the random variable given by the increment $w(t) - w(s)$ is normally distributed with mean zero and variance $t - s$;equivalently,$w(t) - w(s) \sim \sqrt{t - s}N(0,1)$,where $N(0,1)$ denotes a normally distributed random variable with zero mean and unit variance.
- For $0 \leq s < t < u < v \leq T$ the increments $w(t) - w(s)$ and $w(v) - w(u)$ are independent

3.19 Applications of Stochastic Differential Equation

Stochastic differential equation (SDE) models have a wide range of application in areas of Finance, Biology, Chemistry, Epidemiology, Mechanics, Microelectronics, and Economics.

3.20 General Stochastic Differential Equation

Consider an ordinary differential equation of the form

$$\frac{dx(t)}{dt} = f(t, x(t)) \ , X(0) = x_0 \tag{3.19}$$

Suppose we add randomness to the system, then the general stochastic differential equation of (3.19) is of the form

$$\frac{dx(t)}{dt} = f(t, x(t)) + g(t, x(t))\frac{dw(t)}{dt} \tag{3.20}$$

Where $f: < 0, T > \times R \to R$ is the drift coefficient and

$g: < 0, T > \times R \to R$ is the diffusion coefficient.

Multiplying equation (3.20) by dt gives

$$dx(t) = f(t, x(t))dt + g(t, x(t))dw(t), \ X(0) = x_0 \tag{3.21}$$

as the general SDE with initial condition $x(0) = x_0$.

If $x(t)$ solves equation (3.21), then integrating and substituting the initial condition gives

$$X(t) = X(0) + \int_0^t f(s, X(s))ds + \int_0^t g(s, X(s))dw(s)$$

3.21 Stochastic SIR Epidemic Model

Now that the deterministic model is understood, a stochastic version of the SIR model is obtained by random perturbation of the deterministic model with white noise. We Replace the contact rate β in the system (3.13) by $\beta + \rho\frac{d\beta}{dt}$, where $\frac{d\beta}{dt}$ is a white noise (i.e. $B(t)$ is a Brownian motion. See[8], [16], [17], [18]). Hence

$$\frac{1}{N}\left[\frac{ds}{dt}\right] = \mu\frac{N}{N} - \mu\frac{S}{N} - \left(\beta + \rho\frac{d\beta}{dt}\right)\frac{S}{N}.\frac{I}{N}$$

$$\frac{1}{N}\left[\frac{dI}{dt}\right] = \left(\beta + \rho\frac{d\beta}{dt}\right)\frac{S}{N}.\frac{I}{N} - \mu\frac{I}{N} - \gamma\frac{I}{N} \qquad (3.22)$$

$$\frac{1}{N}\left[\frac{dR}{dt}\right] = \gamma\frac{I}{N} - \mu\frac{R}{N}$$

Substituting the fractional variables s, i, r into (3.22) gives

$$\frac{ds}{dt} = \mu - \mu s - \left(\beta + \rho\frac{d\beta}{dt}\right)s.i$$

$$\frac{di}{dt} = \left(\beta + \rho\frac{d\beta}{dt}\right)s.i - \mu i - \gamma i \qquad (3.23)$$

$$\frac{dr}{dt} = \gamma i - \mu r$$

Multiplying system (3.23) by dt and re-arranging gives the stochastic version of the system (3.13) as

$$ds = [\mu - \mu s - \beta si]dt - \rho sid\beta$$

$$di = [\beta si - \mu i - \gamma i]dt + \rho sid\beta \qquad (3.24)$$

$$dr = [\gamma i - \mu r]dt$$

3.22 The Ito-Formula

The Ito-formula is used to solve stochastic differential equations which are difficult to be integrated by the normal integration. Let the Stochastic process $x(t)$ be a solution of the stochastic differential equation

$dx(t) = f\big(t, x(t)\big)dt + g\big(t, x(t)\big)dw(t)$, for some suitable functionsf, g.

Let also $h(t,x)$: $(0,\infty) \times R \to R$ be a twice continuously differentiable function. Then

$Y(t) = h(t, x(t))$, is a stochastic process for which

$$dY(t) = \frac{dh}{dt}\big(t, x(t)\big)dt + \frac{dh}{dx}\big(t, x(t)\big)dx(t) + \frac{1}{2}\cdot\frac{d^2h}{dx^2}\big(t, x(t)\big)(dx(t))^2 \qquad (3.25)$$

Where

$(dx(t))^2 = \big(dx(t)\big).(dx(t))$ is computed according to the rules

$dt.dt = dt.dw(t) = dw(t).dt = 0, \qquad dw(t).dw(t) = dt$

Equation (3.25) is called Ito's formula. (See [2] ,[18],for more on Ito Formula).

3.23 Solving the Stochastic SIR Epidemic Model

Now that the deterministic model is understood, consider the stochastic SIR model of system (3.24). Again the R term is ignored, since it has no effect on the dynamics of S and I. Hence the equivalent system is

$$ds = [\mu - \mu s - \beta si]dt - \rho sid\beta$$

$$di = [\beta si - \mu i - \gamma i]dt + \rho sid\beta \qquad (3.26)$$

3.24 The Disease-Free Equilibrium

In the absence of infection, $i = 0$,Hence system (3.26) reduces to

$$ds = [\mu - \mu s]dt \tag{3.27}$$

3.25 Solving the Stochastic Disease-Free Equilibrium by Ito-Formula

In order to solve the system (3.27), we set $X(t) = S - 1$, so that system (3.27) becomes

$$dX = -\mu X(t).dt \tag{3.28}$$

Now applying the Ito Formula (3.19) to (3.28), we denote $u\big(t, x(t)\big) = e^{\mu t}.X$, and compute its derivative at point $u(t, x(t))$ using the Ito Formula.

$$du\big(t, x(t)\big) = d(e^{\mu t}.X) = X\mu e^{\mu t}.dt + e^{\mu t}.\big(-\mu X(t)\big).dt + 0.d((t))^2 \tag{3.29}$$

$$= X\mu e^{\mu t}.dt - X\mu e^{\mu t}.dt + 0.dt \tag{3.30}$$

Integrating equation (3.30) gives

$$e^{\mu t}.X(t) = c. \tag{3.31}$$

Dividing (3.31) by $e^{\mu t}$ gives the solution

$$X(t) = ce^{-\mu t} \tag{3.32}$$

Substituting the initial condition $X(0) = X_0$ into (3.22) gives

$$X(t) = X_0 e^{-0.0875t} \tag{3.33}$$

But $X(t) = S - 1$, substituting into (3.33) gives

$$S(t) - 1 = (S_0 - 1)e^{-\mu t} \tag{3.34}$$

$$\Rightarrow S(t) = 1 + (S_0 - 1)e^{-\mu t} \tag{3.35}$$

But $S_0 < 1$

$$S(t) = 1 - |S_0 - 1|e^{-\lambda t} \tag{3.36}$$

Let $\sigma_0 = |S_0 - 1|$

Hence $S^*(t) = 1 - \sigma_0 e^{-\lambda t}$ (3.37)

Hence the equilibrium point of the disease-free equilibrium (S^*, I^*) corresponds to $(S^*, I^*) = (1 - \sigma_0 e^{-\mu t}, 0)$.

3.26 Numerical Solution of SDEs-Euler-Maruyama Method

A scaler, autonomous SDE can be written in integral form as

$$X(t) = X_0 + \int_0^t f(s, x(s))ds + \int_0^t g(s, x(s))dw(s), \quad 0 \le t \le T \tag{3.38}$$

Where, f and g are scaler functions and the initial condition x_0 is a random variable.

If $x(t)$ is the solution to (3.38), then the solution $x(t)$ is a random variable that arises when we take the zero stepsize limit in the numerical (method).

Hence the differential equation form of (3.38) can be written as

$$dx(t) = f(t, x(t))dt + g(t, x(t))dw(t), \; X(0) = x_0, \quad 0 \le t \le T \tag{3.39}$$

Hence from equation (3.39), if $g = 0$ and x_0 is constant, then the problem becomes deterministic and (3.39) reduces to ordinary differential equation

$$\frac{dx(t)}{dt} = f(t, x(t)), \text{ with } X(0) = x_0 \tag{3.40}$$

To apply the Euler-Maruyama method to (3.39) over $(0, T)$, we first discretize the interval. Thus we let $\Delta t = \frac{T}{L}$ for some positive integer L and $T_j = j\Delta t$.

Hence our numerical approximation to $X(T_j)$ will be denoted by X_j.Therefore the Euler – Maruyama (EM) method takes the form.

$$X_j = X_{j-1} + f(X_{j-1})\Delta t + g(X_{j-1})(\big(W(T_j) - W(T_{j-1})\big), \; j = 1,2 \ldots \ldots \ldots L \tag{3.41}$$

The equation (3.41) comes from the integral form

$$X(T_j) = X(T_{j-1}) + \int_{T_{j-1}}^{T_j} f(s, x(s))ds + \int_{T_{j-1}}^{T_j} g(s, x(s))dw(s) \tag{3.42}$$

Again if $g = 0$ and x_0 constant, then (3.39) reduces to Euler's Method. (See [32], [33] for more on Euler –Maruyama method).

CHAPTER 4

MODELING AND SIMULATION

4.1 Introduction

In this chapter, the parameter values were fitted into the model and the stability of their equilibrium points determined. Also, numerical simulations of all the models are implemented to explore the behavior of the models.

We acknowledge the difficulty in estimating some of these parameters, since estimates of some of the parameters are complicated and tricky to attain from measurements in real life. However, a thorough search was done in compiling the interesting parameters such as Mortality rate, Rate of infection and Recovery rate from a reliable source.

Table 4.1: Table of parameter values

The parameters	Definition	Parameter Values	Parameter Source
μ	Mortality Rate	0.0875	CIA world factbook
β	Infection Rate	1.5	Ghana Sentinel Survey
γ	Removal Rate	0.029	Ghana Sentinel Survey

4.2 The Deterministic Model Formulation

The parameter values such as mortality rate, infection and removal rates were taken from Ghana Health service and CIA world factbook (demographic statistics), and were fitted into our model in order to determine the equilibrium points as shown in table (4.1).

4.2.1 Equilibrium Points of the Deterministic Model

In order to determine the equilibrium points of the deterministic model, the parameter values were substituted into the deterministic model equations (3.15). Thus,

$$\frac{ds}{dt} = 0.0875 - 0.0875s - 1.5si \tag{4.1}$$

$$\frac{di}{dt} = 1.5si - (0.0875 + 0.029)i \tag{4.2}$$

Applying the equilibrium condition and equating the left-hand side of (4.1) and (4.2) to zero and solving them simultaneously, we have

$$0 = 0.0875 - 0.0875s - 1.5si \tag{4.3}$$

$$0 = 1.5si - (0.1165)i \tag{4.4}$$

From (4.4) $0 = i(1.5s - (0.1165))$, Hence either $i = 0$ or

$$1.5s - 0.1165 = 0$$

$$s = 0.0776$$

Substituting into equation (4.3) produces the disease-free equilibrium point $(s, i) = (1,0)$ and the endemic equilibrium point$(s, i) = (0.0776,0.6927)$.

4.2.2 Stability Analysis of the Deterministic Model at the Disease-free state

The stability analysis in respect of the disease-free equilibrium is as follows.

Let $f(s,i) = 0.0875 - 0.0875s - 1.5si$

$$g(s,i) = 1.5si - (0.0875 + 0.029)i$$

Then the Jacobian of f and g is given by

$$J = \begin{bmatrix} \frac{df}{ds} & \frac{df}{di} \\ \frac{dg}{ds} & \frac{dg}{di} \end{bmatrix} = \begin{bmatrix} -0.0875 - 0.66i & -1.5s \\ 1.5i & 1.5s - (0.1165) \end{bmatrix}$$

Therefore

$$J(s,i) = J(1,0) = \begin{bmatrix} -0.0875 & -1.5 \\ 0 & 1.3835 \end{bmatrix}$$

The characteristics equation is given by

$$\lambda^2 - 1.296\lambda - 0.121056 = 0$$

Hence $\lambda_1 = 1.3835$ and $\lambda_2 = -0.0875$

Since the eigenvalues are of opposite signs, the equilibrium point is a saddle point. Hence the equilibrium point $(s,i) = (1,0)$ is an unstable equilibrium point.

4.2.3 Stability Analysis of the Deterministic Model at the Endemic State

The stability analysis in respect of the endemic equilibrium is given as follows

Let $f(s,i) = 0.0875 - 0.0875s - 1.5si$

$g(s,i) = 1.5si - (0.0875 + 0.029)i$

Then the Jacobian of f and g is given by

$$J = \begin{bmatrix} \frac{df}{ds} & \frac{df}{di} \\ \frac{dg}{ds} & \frac{dg}{di} \end{bmatrix} = \begin{bmatrix} -0.0875 - 0.66i & -1.5s \\ 1.5i & 1.5s - (0.1165) \end{bmatrix}$$

The Jacobian at the equilibrium point $(s, i) = (0.077666, 0.692746)$ is given by

$$J(s,i) = J(0.0776, 0.6927) = \begin{bmatrix} -1.1266 & -1.1165 \\ 1.0391 & -0.000001 \end{bmatrix}$$

Hence the characteristic equation is

$$\lambda^2 + 1.1266\lambda + 1.1601 = 0$$

The eigenvalues are given by $\lambda_1 = -0.5633 + 0.9180i$ and $\lambda_2 = -0.5633 - 0.9180i$

The equilibrium point of the endemic equilibrium is a spiral equilibrium point. For spiral equilibrium point, its stability is determined by the real part. Since the real parts are both negative, the endemic equilibrium is stable.

4.3 The Stochastic Model Formulation

Here, the parameter values from table 4.1 were also fitted into the stochastic model equations (3.26) and the equilibrium point of the disease-free equilibrium determined.

Specifically, the parameter values of mortality rate, infection rate and removal rate were substituted into (3.26) to yield

$$ds = [0.0875 - 0.0875s - 1.5si]dt - \rho sid\beta \quad (4.5)$$

$$di = [1.5si - 0.0875i - 0.029i]dt + \rho sid\beta \quad (4.6)$$

4.3.1 The Equilibrium point of the Stochastic Model at the Disease-Free State

In the absence of infection, $i = 0$, Hence the system becomes

$$ds = [0.0875 - 0.0875s]dt \quad (4.7)$$

Setting $X(t) = S - 1$, system (4.7) becomes

$$dX = -0.0875.X(t).dt \tag{4.8}$$

Again applying the Ito Formula (3.19) to (4.8), we denote $(t, x(t)) = e^{0.0875t}.X$, and compute its derivative at point $u(t, x(t))$ using the Ito Formula

$$du(t, x(t)) = d(e^{0.0875t}.X) = 0.0875Xe^{0.0875t}.dt - 0.0875Xe^{0.0875t}.dt + 0.dt \tag{4.9}$$

Integrating equation (4.9) gives

$$e^{0.0875t}X = c \tag{4.10}$$

Dividing (4.10) by $e^{0.0875t}$ gives

$$X(t) = ce^{-0.0875t} \tag{4.11}$$

Substituting the initial condition $X(0) = X_0$ into (4.11) gives

$$X(t) = X_0e^{-0.0875t} \tag{4.12}$$

But $X(t) = S - 1$, substituting into (4.12) gives

$S(t) - 1 = (S_0 - 1)e^{-0.0875t}$, re-arranging gives

$$S(t) = 1 + (S_0 - 1)e^{-0.0875t} \tag{4.13}$$

But $S_0 < 1$

Hence $S(t) = 1 - |S_0 - 1|e^{-0.0875t}$ (4.14)

Let $\sigma_0 = |S_0 - 1|$

$S^*(t) = 1 - \sigma_0 e^{-0.0875t}$

Hence the equilibrium point of the disease-free equilibrium (S^*, I^*) corresponds to $(S^*, I^*) = (1 - \sigma_0 e^{-0.0875t}, 0)$.

4.4 Numerical Simulations

Numerical simulations are vital tools for analyzing the disease progression patterns. Our numerical results were obtained using MATLAB, by means of some epidemiological parameter values, obtained from reliable sources. Since some of our parameter values were taken from Ghana where data keeping is poor, the infection rate was varied whilst the other parameters were unchanged for the purpose of our simulation. We therefore perform simulation of the deterministic and stochastic models and compare them.

4.4.1 Simulations of the Deterministic Model

A numerical simulation of the deterministic Model (equations (4.1) and (4.2)) was performed using initial conditions of $(0) = 0.99$, $I(0) = 0.01$ and the parameter values of $\mu = 0.0875$, $\beta = 1.5$, $\gamma = 0.029$. A plot of S, I against time yielded by the simulation is displayed in Figure 4.1. We observe from the figure that about 72 percent of the population would be infective , 8 percent would be susceptible and about 20 percent would be removed, at the end of the time frame of about 25 years. The endemic equilibrium point computed in section 4.2.1 confirmed this result with the same set of parameter values. The endemic equilibrium estimates that about 8 percent would be susceptible and 70 percent would be infective in the same time period. The crossover point after which the number of infectives permanently exceeds the number of susceptibles occurs at about year 3.5.

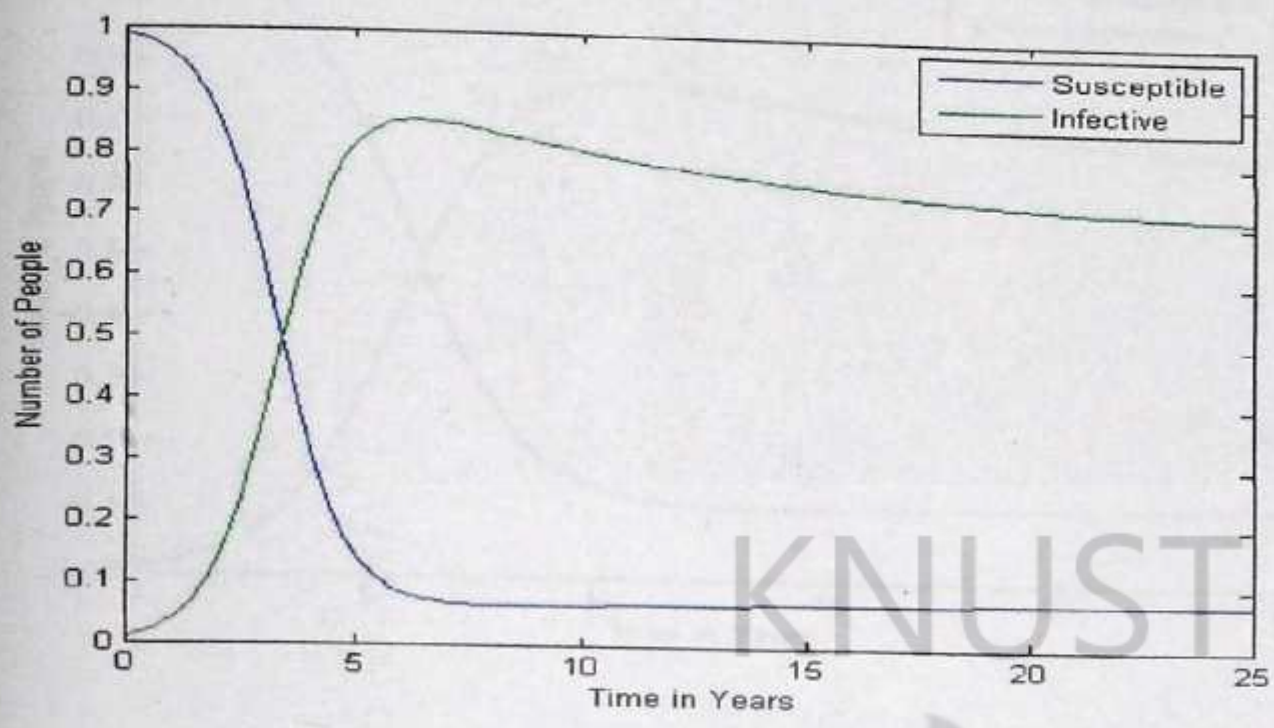

Figure 4.1: A Computer Simulation of the Deterministic Model (4.1 and 4.2).

4.4.2 Simulations of the Deterministic Model with reduced Infection Rate

A numerical simulation of the deterministic Model was performed using initial conditions of $S(0) = 0.99$, $I(0) = 0.01$ and the same parameter values except for a reduced infection rate of $\beta = 0.9$. A plot of S, I against time yielded by the simulation is displayed in Figure 4.2. Again with the same set of parameter values, but different infection rate of $\beta = 0.9$. The deterministic model plot of figure 4.2 now shows slightly different issue. A lower percentage of the population would be infected, and higher percentage would be susceptible in the same period of time. Thus 68 percent would be infected and about 13 percent would be susceptible whilst about 19 percent would be removed. . The crossover point after which the number of infectives permanently exceeds the number of susceptibles occurs at about year 7.

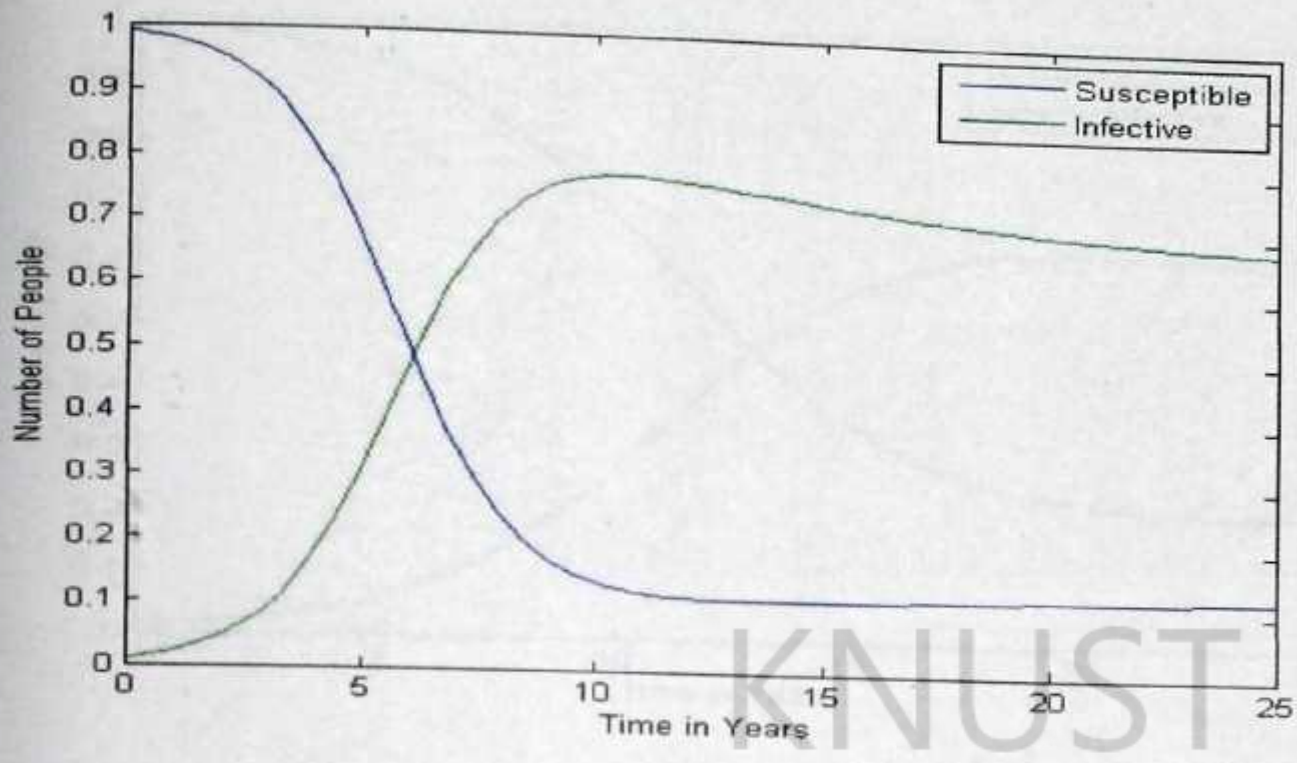

Figure 4.2: A Computer simulation of the Deterministic Model with a lower infection rate of $\beta = 0.9$.

4.4.3 Simulations of the Deterministic Model with further reduced Infection Rate

A numerical simulation of the deterministic Model was performed using initial conditions of $(0) = 0.99$, $I(0) = 0.01$ and the same parameter values except for a further reduced infection rate of $\beta = 0.5$. A plot of S, I against time yielded by the simulation is displayed in Figure 4.3. The deterministic model plot of figure 4.3 now shows slightly different issue: that 62 percent of the population would be infected, and almost 22 percent would be susceptible, with 16 percent removed in 25years. The crossover point after which the number of infectives permanently exceeds the number of susceptibles occurs at about year 13.

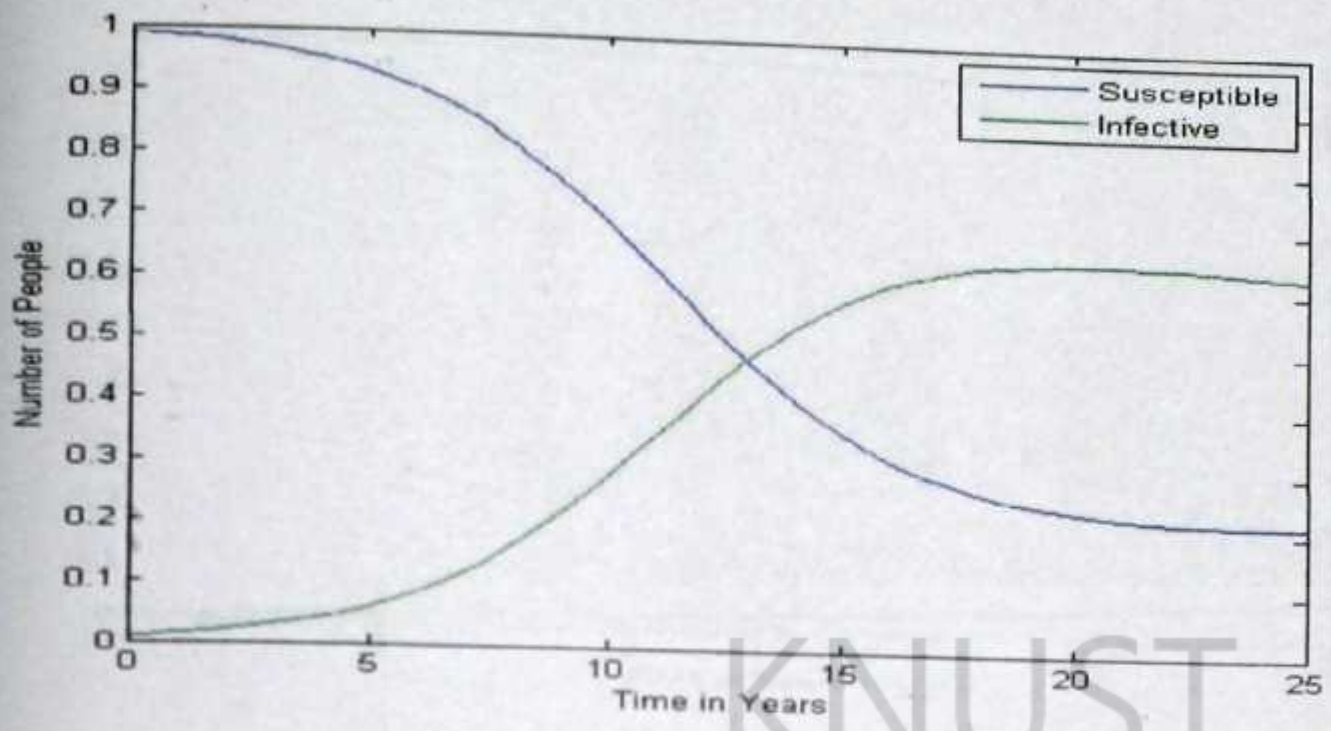

Figure 4.3: A computer simulation of the Deterministic Model with a lower infection rate of $\beta = 0.5$

4.4.4 Simulations of the Deterministic Model with sufficiently reduced Infection Rate

A numerical simulation of the deterministic Model was performed using initial conditions of $(0) = 0.99$, $I(0) = 0.01$ and the same parameter values except for a much reduced infection rate of $\beta = 0.2$. A plot of S, I against time yielded by the simulation is displayed in Figure 4.4. The deterministic model plot of figure 4.4 now shows a much improved situation: With the infection rate of $\beta = 0.2$, the simulation showed that about 92 percent of the population would be susceptible and about 8 percent of the population would be infected within the time frame of over 25 years and the populations would not crossover.

Thus the number of infectives permanently be less than the number of susceptibles indicating that an infection rate of $\beta = 0.2$ is sufficiently low.

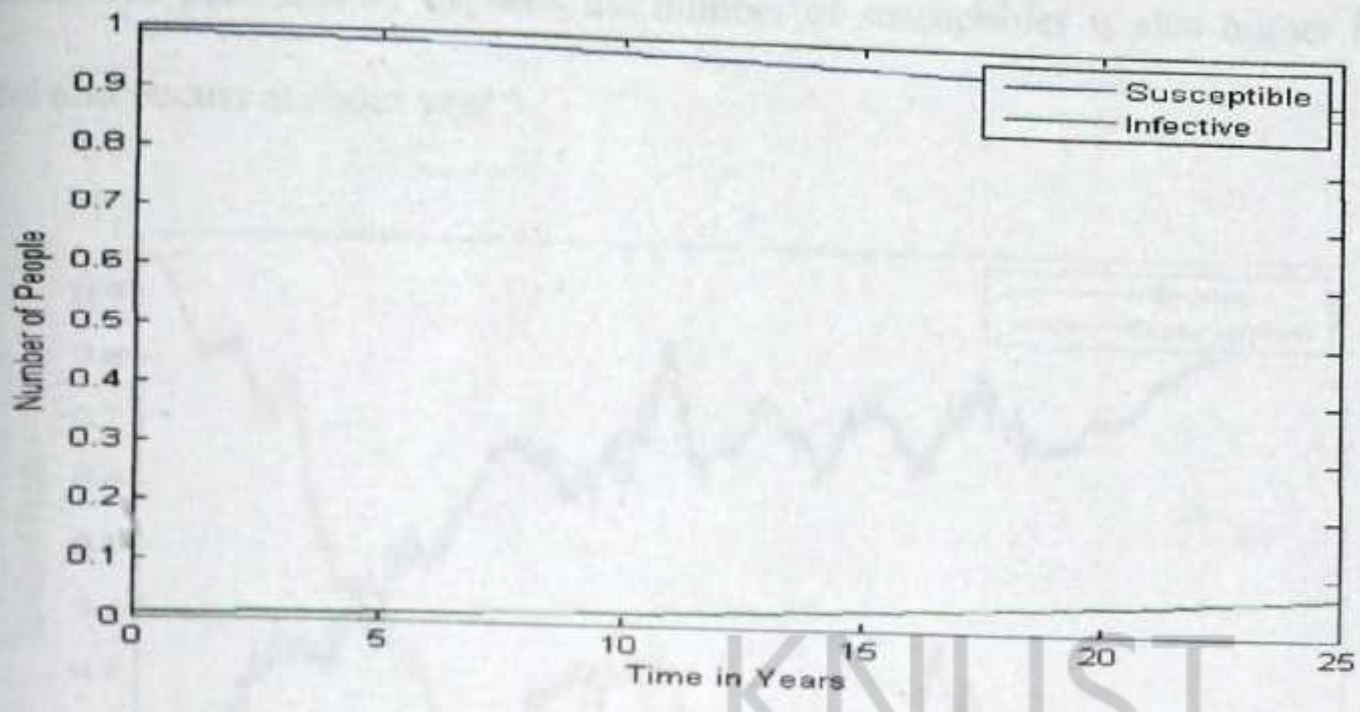

Figure 4.4: A computer simulation of the Deterministic Model with a lower infection rate of $\beta = 0.2$

4.5 Numerical Simulations of the Stochastic Model

4.5.1 Simulations of the Stochastic Model with the Original Parameter values

A numerical simulation of the stochastic model (equations (4.5) and (4.6)) was performed using initial conditions of $(0) = 0.99$, $I(0) = 0.01$ and the parameter values of $\mu = 0.0875$, $\beta = 1.5$, $\gamma = 0.029$. A plot of S, I against time yielded by the simulation is displayed in Figure 4.5. We observe from the figure that about 90 percent of the population would be infective , 8 percent would be susceptible and about 2 percent would be removed, at the end of the time frame of about 25 years. The endemic equilibrium point computed in section 4.2.2 is not quite in agreement with this result even with the same set of parameter values. (For the deterministic model, the endemic equilibrium estimates that about 8 percent would be susceptible and 72 percent would be infective in the same time period). The crossover point after which the number

of infectives permanently exceeds the number of susceptibles is also higher for the stochastic model and occurs at about year 5.

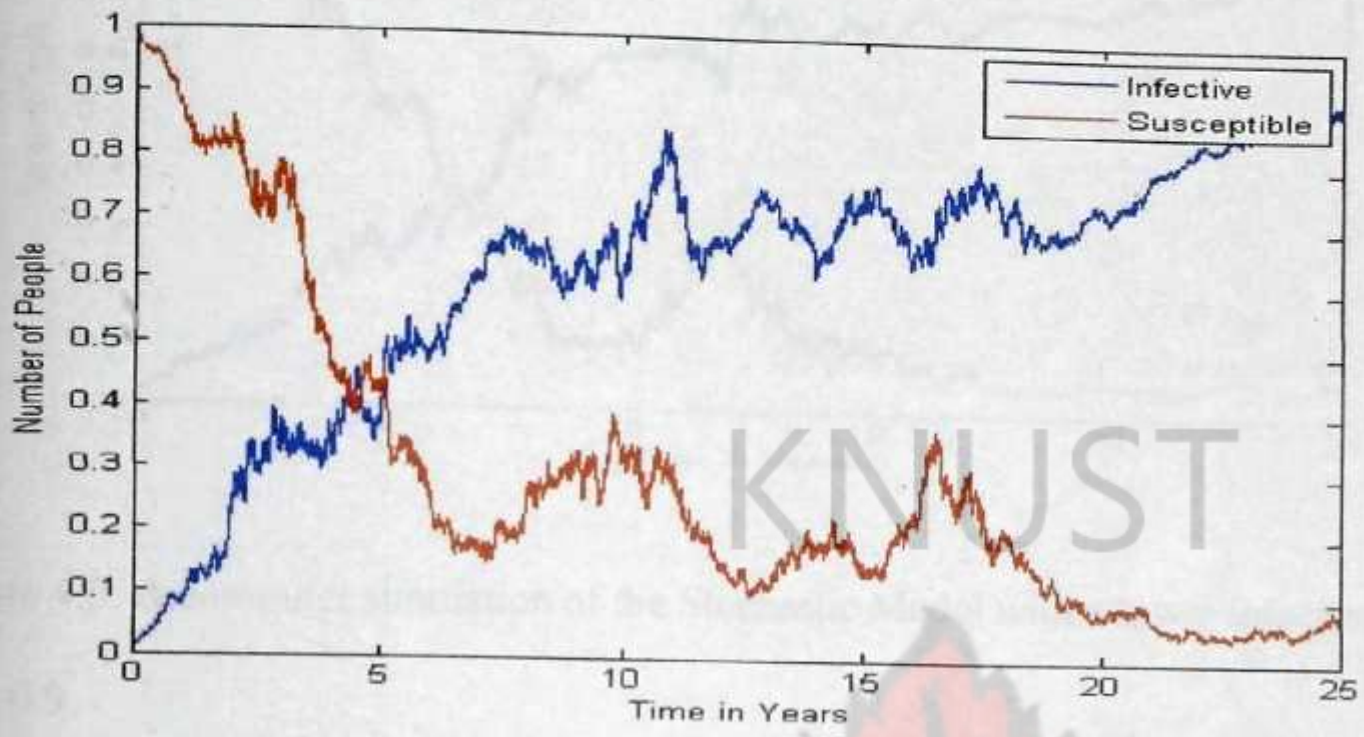

Figure 4.5: A computer simulation of the Stochastic Model with original parameter values

4.5.2 Simulations of the Stochastic Model with Reduced Infection Rate

A numerical simulation of the stochastic model (equations (4.5) and (4.6)) was performed using initial conditions of $(0) = 0.99$, $I(0) = 0.01$ and the same parameter values except that the infection rate is reduced to $\beta = 0.9$,. A plot of S, I against time yielded by the simulation is displayed in Figure 4.6. The stochastic model plot again shows that about 80 percent of the population would be infective, 8 percent would be susceptible and about 12 percent would be removed in the same time frame compared to 68%, 12% and 22% respectively for the deterministic model.

The crossover point after which the number of infectives permanently exceeds the number of susceptibles is also the same for the stochastic model and occurs at about year 7.

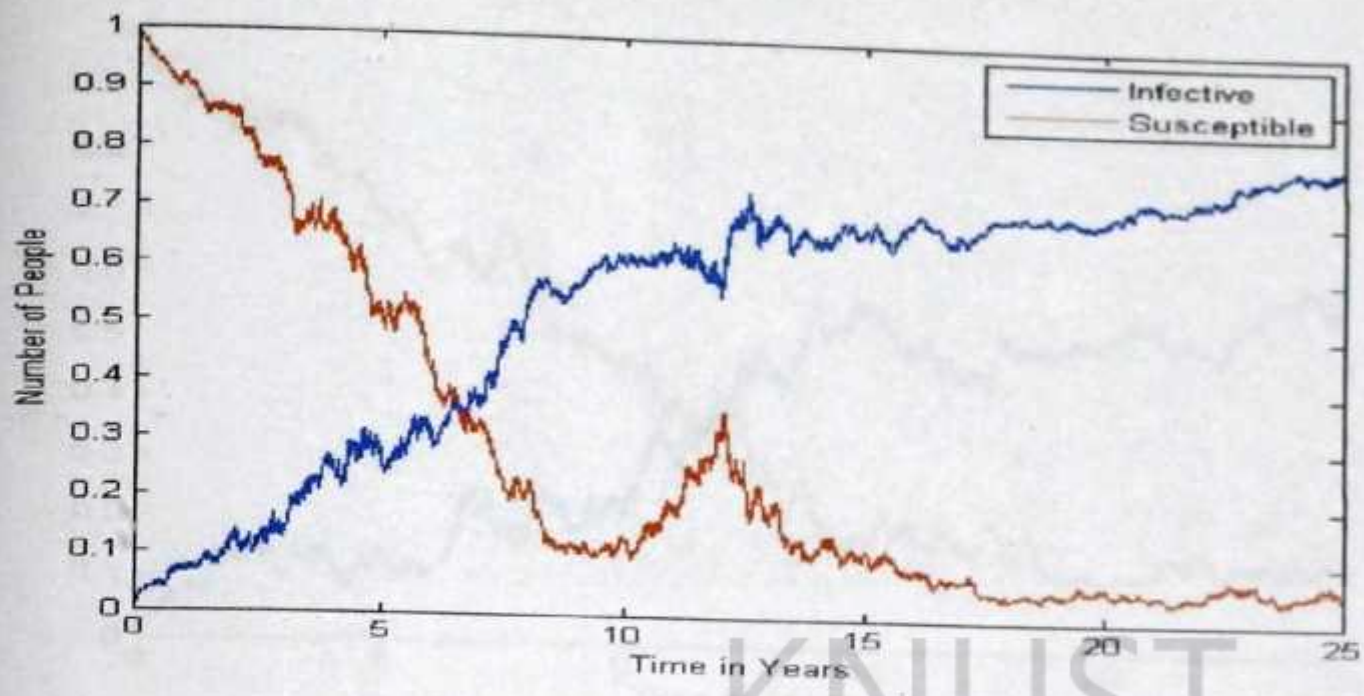

Figure 4.6: A computer simulation of the Stochastic Model with a lower infection rate of $\beta = 0.9$

4.5.3 Simulations of the Stochastic Model with further reduced Infection Rate

A numerical simulation of the stochastic Model was performed using initial conditions of $(0) = 0.99$, $I(0) = 0.01$ and the same parameter values except for a further reduced infection rate of $\beta = 0.5$. A plot of S, I against time yielded by the simulation is displayed in Figure 4.7. The stochastic model plot of figure 4.7 now shows slightly different issue: that 60 percent of the population would be infected, and almost 18 percent would be susceptible, with 22 percent removed in 25years. The crossover point after which the number of infectives permanently exceeds the number of susceptibles occurs at about year 13 and is about the same for the deterministic model.

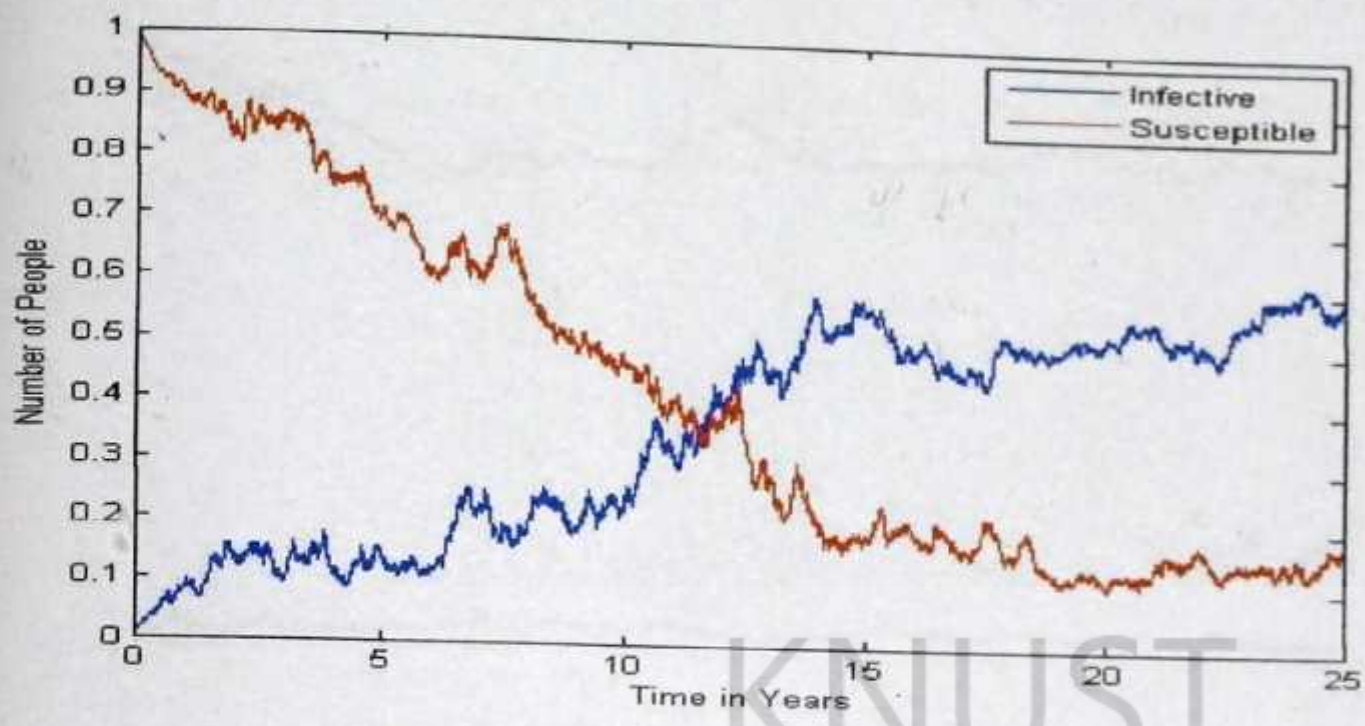

Figure 4.7: A computer simulation of the Stochastic Model with a lower infection rate of $\beta = 0.5$

4.5.4 Simulations of the Stochastic Model with sufficiently reduced Infection Rate

A numerical simulation of the stochastic model was performed using initial conditions of $(0) = 0.99$, $I(0)$ =0.01 and the same parameter values except for a much reduced infection rate of $\beta = 0.2$. A plot of S, I against time yielded by the simulation is displayed in Figure 4.8. The stochastic model plot of figure 4.8 now shows a much improved situation: With the infection rate of $\beta = 0.2$, the simulation showed that about 82 percent of the population would be susceptible and about 3 percent of the population would be infected and 15 percent removed within the time frame of over 25 years and the populations would not crossover.

Thus the number of infectives would be permanently less than the number of susceptibles indicating that an infection rate of $\beta = 0.2$ is sufficiently low for the stochastic model as well.

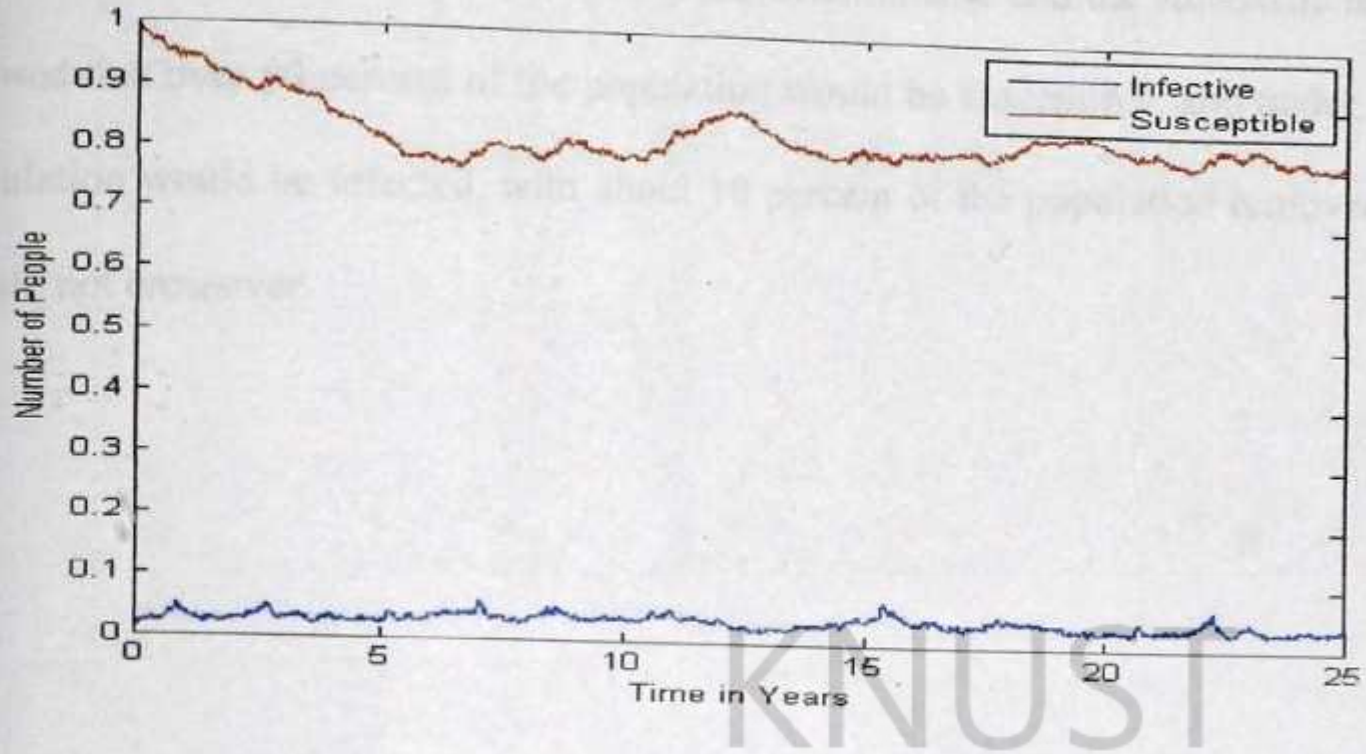

Figure 4.8: A computer simulation of the Stochastic Model with a lower infection rate of $\beta = 0.2$

4.6 Summary of Discussion on Simulations

The stochastic model simulations are generally in agreement with the deterministic model ones in terms of the population crossovers. The dynamics of the HIV disease are represented by deterministic model figures 4.1, 4.2, 4.3, 4.4 and the stochastic model figures 4.5, 4.6, 4.7, 4.8. The graphs showed that at the outbreak of the disease, the infected population starts small, and then as we have random and constant interaction between the infectives and the susceptibles, more people get infected and hence the infectives curve rises quickly. The susceptible curve decreases as a result of more people becoming infected and moving from the susceptible class to the infective class. The graphs showed that in the long term the infected individuals do not vanish from the population, and this corresponds to the endemic equilibrium. To investigate the effect of varying the infection rate on our model, β was given different sets of values. The plots showed that an increase in the infection rate increases the number of infectives in the population, and a decrease in the infection rate decreases the number of infectives.

With the infection rate of $\beta = 0.2$, both the deterministic and the stochastic model simulations showed that over 80 percent of the population would be susceptible, and under 10 percent of the population would be infected, with about 10 percent of the population removed, and the curves would not crossover.

CHAPTER 5

CONCLUSION AND RECOMMENDATIONS

5.1 INTRODUCTION

The work began with a study of the epidemiology of HIV disease. We then reviewed mathematical models of infectious diseases. The dynamics of dynamical systems of differential equations were then discussed, with the interest in equilibrium points, phase portrait and solution paths, since these are important tools in describing solutions of Differential equations analytically. This was then applied to our model, the SIR epidemic model. Stochastic version of the SIR epidemic model was then introduced and analyzed.

5.2 SUMMARY

The selected models considered here were motivated by the general nature of HIV and dynamical modeling initiatives and is not our desire to present a comprehensive account of mathematical models available till date. There was an urgent need for extensive mathematical models of AIDS incidence and spread so as to enable informed efficient investments in preventive therapeutic measures. Our work concentrates on spread of HIV in Ghana.

From our epidemiological perspective R_0 is an important indicator of the initial causes of HIV, and the infection rate has large effect on the spread of HIV in Ghana. The computer-simulated results can be adapted to project future occurrence of the disease.

Our deterministic plot of figure 4.1 showed that about 72 percent of the population would be infective, 8 percent would be susceptible and about 20 percent would be removed, within the time frame of over 25 years.

The endemic equilibrium point confirmed this result with the same set of parameter values. The endemic equilibrium estimates that about 8 percent would be susceptible and 70 percent would be infective in the same time period.

Again with the same set of parameter values, but different infection rate of $\beta = 0.9$, the deterministic plot of figure 4.2 shows slightly different issue. A lower percentage of the population would be infected, and higher percentage would be susceptible in the same period of time. Thus 68 percent would be infected and about 13 percent would be susceptible whilst about 19 percent be removed.

When the infection rate was changed to $\beta = 0.5$, the computer-simulated results showed that 62 percent of the population would be infected, and almost 22 percent would be susceptible ,with 16 percent removed within the time frame of over 25 years.

With sufficiently lower infection rate of $\beta = 0.2$, the simulation showed that about 92 percent of the population would be susceptible and about 8 percent of the population would be infected and the population would not crossover.

The stochastic simulations have apparent stochastic behavior and that the overall trend of the trajectories follows the same path as that of the deterministic ones. This means that even though fluctuations occur, they result in the same behavior as the deterministic model. The deterministic approach has limitations that the stochastic approach handles in a more realistic way.

The deterministic approach gives the same result every time the simulation is run with the same initial values. This might be mathematically correct, but this is not the case in a real epidemic situation. This is due to the fact that there may exist many parameters which we cannot model entirely realistically; by modeling them deterministically we lose some of the complexity of the system. It is therefore appropriate to assume a stochastic behavior.

Our stochastic simulation of figure 4.4 shows that 90 percent of the population would be infected, and 8 percent would be susceptible and about 2 percent would be removed in the same time frame as the deterministic one.

When the infection rate was changed to $\beta = 0.9$, the stochastic simulation reveals that 80 percent would be infected, about 8 percent would be susceptible, and about 12 percent would be removed within time frame of 25 years.

The stochastic plot again shows that about 60 percent of the population would be infective, 18 percent would be susceptible and about 22 percent would be removed when the infection rate is $\beta = 0.5$ in the same time frame.

With sufficiently lower infection rate of $\beta = 0.2$, the stochastic simulation showed that about 82 percent of the population would be susceptible , about 3 percent of the population would be infected, 15 percent of the population would be removed, and the population would not crossover.

The stochastic simulations seem to give a higher percentage of infective population with the same set of parameter values as compared to the deterministic simulations. This is due to the fact that the deterministic model is insensitive to stochastic variation which occurs in actual population naturally.

5.3 CONCLUSION

In this thesis, we studied epidemiological models of HIV for both Deterministic and Stochastic approaches. Since equilibrium points are important tools in performing stability analysis of infectious disease models, we determined the two equilibrium points. Thus the disease-free equilibrium and the endemic equilibrium point for the deterministic model and the disease-free

equilibrium point for the stochastic model. The stability of these equilibrium points were then determined.

In order to make our model reflect reality, our parameter values were obtained from Ghana and were fitted into the model, and their stability at the equilibrium points was then determined.

The results showed an unstable disease-free equilibrium and a stable endemic equilibrium. This is true in this case, since for the disease-free to be stable $R_0 < 1$ and $R_0 > 1$ for the endemic equilibrium to be stable. Our results showed R_0 for both the disease-free and endemic to be greater than 1.

Hence, we see the importance of the mathematical model as they can be used to explore and identify the types of data that needs to be collected and the parameter values that need to be accessed.

To conclude, we say that, though it is practically impossible to achieve a disease-free state in Ghana, yet efforts have to be made in eradicating HIV/AIDS, since many talented individuals and vibrant manpower have been lost due to the disease. The model showed that if we could reduce the infection rate drastically, then more people can be prevented from getting infected. Since reducing the infection rate reduces the infective population. The model showed that it will be difficult to get to disease-free state. This is due to the fact that the disease-free was unstable and that there is always a constant and random interactions between the susceptible and infected individuals, and that each individual have equal chance of contacting any other individual in the whole population during a given time period, as individuals move rapidly and at random throughout the population. The models also allowed us to determine the spread of HIV and the

stability of AIDS in Ghana. It also allowed us to have an insight about the future occurrence of the disease and also to put in place strategic policies to avert the spread of the disease.

5.4 RECOMMENDATIONS

- The model did not include the endemic equilibrium of the stochastic model since it was a bit complicated. Even though the endemic equilibrium of the stochastic model was not determined, its numerical simulation was performed in order to compare with the deterministic simulation. We therefore recommend that further research is to be extended to include the stochastic endemic equilibrium.
- The model assumed a homogenous constant population. We recommend that further research would be extended to include a heterogeneous mixing pattern in the population, because several studies have shown that averaging, the mixing patterns of heterogeneous population can cause R_0 to decrease or remain unaltered. Thus , if we determine the mixing patterns in population, we can obtain better estimates of R_0. This result can help modelers predict the severity of an outbreak and the best means of containing it.
- We recommend that public health campaigns should increase in order to make people informed about the need of abstinence, condom use, and faithfulness in order to reduce the infection rate to as low as $\beta = 0.2$, in order to prevent population crossover. The simulations showed that an infection rate of $\beta = 0.2$ would prevent the populations from crossing over. This is due to the fact that as the infection rate increases, more percent of population get infected, and as the infection rate reduces, the percentage of the infectives in the population also reduces. Hence the need to reduce the infection rate.
- The government must put in place legislation on some health care delivery to control the spread of HIV/AIDS through opportunistic sex, unhygienic instrument, blood transfusion

etc. the cost evaluation suggest that huge amount of money is needed to support small percentage of the infectives in any given population with the HIV/AIDS

- We recommend that intensive educational program and proper policy decisions would be carried out which may include the promotion of the widespread availability of prophylactics and the increased availability of drugs such as AZT in order to increase the removal rate through better medical treatment of the infected individuals.

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APPENDIX

Existence and Uniqueness of Stochastic Differential Equation

Theorem: Suppose that b and B are continuous and satisfy the following conditions

a) $|b(x,t) - b(\dot{x},t)| \leq L|x - \dot{x}|$

$|B(x,t) - B(\dot{x},t)| \leq L|x - \dot{x}|$, for all $0 \leq t \leq T, x, \dot{x} \in R^n$

b) $|b(x,t)| \leq L(1 + |x|)$

$|B(x,t)| \leq L(1 + |x|)$, for all $0 \leq t \leq T, x \in R^n$

For some constant L, let x_0 be any R^n-valued random variable such that

c) $E(|x_0|^2) < \infty$

and

d) x_0 is independent of $W^+(\theta)$,where $w(\cdot)$ is s given m-dimensional Brownian motion, then there exists a unique solution $x \in Ln^2(0,T)$ of the stochastic differential equation:

$$\begin{cases} dx = b(x,t)dt + B(x,t)dw \;\; 0 \le t \le T \\ x(0) = x_0 \end{cases} \tag{1.1}$$

Proof 1: Uniqueness

Suppose x and $\dot{x}$ are solutions of equation (1.1), then for all $0 \le t \le T \quad x(t) - \dot{x}(t) =$

$\int_0^t b(x,s) - b(\dot{x},s)ds + \int_0^t B(x,s) - B(\dot{x},s)dw$

Since $(a+b)^2 \le 2a^2 + 2b^2$,then we can estimate

$$E(|x(t) - \dot{x}(t)|^2) \le 2E\left(\left|\int_0^t b(x,s) - b(\dot{x},s)ds\right|^2\right)$$

$$+2E(\left|\int_0^t B(x,s) - B(\dot{x},s)dw\right|^2)$$

the Cauchy-Schwarz inequality implies that

$$\left|\int_0^t f ds\right|^2 \le t\int_0^t |f|^2 ds$$

for any $t > 0$ and $f: [0,t] \to R^n$. We use this to estimate

$$E(\left|\int_0^t b(x,s) - b(\dot{x},s)ds\right|^2) \le TE(\int_0^t |b(x,s) - b(\dot{x},s)|^2 ds)$$

$$\le L^2 T \int_0^t E(|x - \dot{x}|^2)ds$$

Furthermore

$$E\left(\left|\int_0^t B(x,s) - B(\dot{x},s)dw\right|^2\right) = E(\int_0^t |B(x,s) - B(\dot{x},s)|^2 ds$$

$$\leq L^2 \int_0^t E(|x - \dot{x}|^2)ds$$

Therefore for some appropriate constant k gives

$E(|x(t) - \dot{x}(t)|^2) \leq k \int_0^t E(|x - \dot{x}(t)|^2)ds$, provided $0 \leq t \leq T$.

Setting $\mu(t) = E(|x(t) - \dot{x}(t)|^2)$, gives $\mu(t) \leq k \int_0^t \mu(s)ds$ for all $o \leq t \leq T$.

By gronwall's lemma, if $k_0 = 0$,implies $\mu = 0$.Thus $x(t) = \dot{x}(t)$ for all $0 \leq t \leq T$, and so $x(r) = \dot{x}(r)$ for all rational $0 \leq r \leq T$,except for some set of probability zero. As x and $\dot{x}$ have continuous sample paths almost surely.

Hence $p(\max_{0 \leq t \leq T}|x(t) - \dot{x}(t)| > 0) = 0$.

Proof 2: Existence

Define iteratively

$$\begin{cases} x^0(t) = x_0 \\ x^{n+1}(t) = x_0 + \int_0^t b(x^n(s)\dot{x},s)ds + \int_0^t B(x^n(s),s)dw \end{cases}$$

For $n = 0,1 \ldots \ldots \ldots$ and $0 \leq t \leq T$.

Define also

$d^n(t) = E(|x^{n+1}(t) - x^n(t)|^2$

We claim that

$d^n(t) \leq \frac{(Mt)^{n+1}}{(n+1)!}$ for all $n = 0, \ldots\ldots, 0 \leq t \leq T$

For some constant M,depending on L, T and x_0 and for $n = 0$, we have

$d^0(t) = E(|x^1(t) - x^0(t)|^2)$

$$= E\left(\left|\int_0^t b(x_0,s)ds + \int_0^t B(x_0,s)dw\right|^2\right)$$

$$\leq 2E\left(\left|\int_0^t L(1 + |x_0|\,ds\right|^2\right) + 2E\left(\int_0^t L^2(1 + |x_0|^2)ds\right)$$

$\leq tM.$

For some large enough constant M.this confirms the claim for $n = 0$

Next assume the claim is valid for some $n - 1$.

Then

$d^n(t) = E(|x^{n+1}(t) - x^n(t)|^2$

$$= E\left(\left|\int_0^t b(x^n,s) - b(x^{n-1},s)ds + \int_0^t B(x^n,s) - B(x^{n-1},s)dw\right|^2\right)$$

$\leq 2TL^2E(\int_0^t |x^n - x^{n-1}|^2 ds)$

$\leq 2L^2(1 + T)\int_0^t \frac{M^n s^n}{n!} ds$ by induction

$$\leq \frac{M^{n+1}t^{n+1}}{(n+1)!}$$

Provided we choose $M \geq 2L^2(1+T)$.this proves the claim.